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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  FEB 25  CA/CAPLUS - Russian Agency for Patents and Trademarks
                  (ROSPATENT) added to list of core patent offices covered
 NEWS  4  FEB 28  PATDPAFULL - New display fields provide for legal status
                  data from INPADOC
 NEWS  5  FEB 28  BABS - Current-awareness alerts (SDIs) available
 NEWS  6  FEB 28  MEDLINE/LMEDLINE reloaded
 NEWS  7  MAR 02  GBFULL: New full-text patent database on STN
 NEWS  8  MAR 03  REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS  9  MAR 03  MEDLINE file segment of TOXCENTER reloaded
 NEWS  10 MAR 22  KOREAPAT now updated monthly; patent information enhanced
 NEWS  11 MAR 22  Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS  12 MAR 22  PATDPASPC - New patent database available
 NEWS  13 MAR 22  REGISTRY/ZREGISTRY enhanced with experimental property tags
 NEWS  14 APR 04  EPFULL enhanced with additional patent information and new
                  fields
 NEWS  15 APR 04  EMBASE - Database reloaded and enhanced

 NEWS EXPRESS  JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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FILE 'HOME' ENTERED AT 12:06:09 ON 04 APR 2005

=> file uspatful
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
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FILE 'USPATFULL' ENTERED AT 12:06:16 ON 04 APR 2005
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 31 Mar 2005 (20050331/PD)
FILE LAST UPDATED: 31 Mar 2005 (20050331/ED)
HIGHEST GRANTED PATENT NUMBER: US6874161
HIGHEST APPLICATION PUBLICATION NUMBER: US2005071904
CA INDEXING IS CURRENT THROUGH 31 Mar 2005 (20050331/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 31 Mar 2005 (20050331/PD)
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REVISED CLASS FIELDS (/NCL) LAST RELOADED: Feb 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Feb 2005

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>>> the earliest to the latest publication. <<<

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substance identification.

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=> e paranhos-baccala g/in
E1            1     PARANG KEYKAVOUS/IN
E2           12     PARANHOS BACCALA GLAUCIA/IN
E3            0 --> PARANHOS-BACCALA G/IN
E4            1     PARANICAS PETER C/IN
E5            1     PARANJAPE ANAND S/IN
E6            1     PARANJAPE MAKARAND/IN
E7           10     PARANJAPE SUSHAMA M/IN
E8            4     PARANJAPE SUSHAMA MAHESH/IN
E9            2     PARANJPE AJIT/IN
E10          34     PARANJPE AJIT P/IN
E11           4     PARANJPE AJIT PRAMOD/IN
E12           1     PARANJPE AJIT PRAMOND/IN

=> s e2
L1           12 "PARANHOS BACCALA GLAUCIA"/IN

=> d l1,cbib,1-12

L1   ANSWER 1 OF 12  USPATFULL on STN
2004:292252 Method for in vitro culture of viruses of the togaviridae and
    flaviviridae families and uses.
    Andre, Patrice, Lyon, FRANCE
    Lotteau, Vincent, Vourles, FRANCE
    Paranhos-Baccala, Glaucia, Lyon, FRANCE
    Komurian-Pradel, Florence, Poleymieux, FRANCE
    Bio Merieux, Marcy L'Etoile, FRANCE (non-U.S. corporation)Institut National
    De La Sante Et De La Recherche Medicale, Paris, FRANCE (non-U.S.
    corporation)
    US 2004229336 A1 20041118
    APPLICATION: US 2004-776617  A1  20040212 (10)
    PRIORITY: FR 1999-10095  19990730
    DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
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L1 ANSWER 2 OF 12 USPATFULL on STN
2004:63780 Endogeneous nucleic fragment associated with an autoimmune disease, labeling method and reagent.
Paranhos-Baccala, Glaucia, Lyon, FRANCE
Mallet, Francois, Villeurbanne, FRANCE
Voisset, Cecile, London, UNITED KINGDOM
BIO MERIEUX, MARCY L'ETOILE, FRANCE (non-U.S. corporation)
US 2004048298 A1 20040311
APPLICATION: US 2003-632793 A1 20030804 (10)
PRIORITY: FR 1999-888 19990121
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 3 OF 12 USPATFULL on STN
2004:57379 The LTR region of MSRV-1 and the proteins it encodes and probes and methods for detecting MSRV-1 retrovirus.
Paranhos-Baccala, Glaucia, Lyon, FRANCE
Perron, Herve, Lyon, FRANCE
Komurian-Pradel, Florence, D'Or, FRANCE
Bio Merieux, Marcy L'Etoile, FRANCE, F-69280 (non-U.S. corporation)
US 2004043381 A1 20040304
APPLICATION: US 2003-637565 A1 20030811 (10)
PRIORITY: EP 1999-420041 19990215
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 4 OF 12 USPATFULL on STN
2003:282306 Viral material and nucleotide fragments associated with multiple sclerosis, for diagnostic, prophylactic and therapeutic purposes.
Perron, Herve, Lyon, FRANCE
Beseme, Frederic, Villefontaine, FRANCE
Bedin, Frederic, Lyon, FRANCE
Paranhos-Baccala, Glaucia, Lyon, FRANCE
Komurian-Pradel, Florence, Saint Cyr au Mont d'Or, FRANCE
Jolivet-Reynaud, Colette, Bron, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Garson, Jeremy Alexander, Guildford, UNITED KINGDOM
Tuke, Philip William, London, UNITED KINGDOM
BIO MERIEUX, L'Etoile, FRANCE (non-U.S. corporation)
US 2003198647 A1 20031023
APPLICATION: US 2002-114104 A1 20020403 (10)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 5 OF 12 USPATFULL on STN
2003:265376 Viral material and nucleotide fragments associated with multiple sclerosis, for diagnostic, prophylactic and therapeutic purpose.
Perron, Herve, Lyon, FRANCE
Beseme, Frederic, Villefontaine, FRANCE
Bedin, Frederic, Lyon, FRANCE
Paranhos-Baccala, Glaucia, Lyon, FRANCE
Komurian-Pradel, Florence, Saint Cyr Au Mont D'or, FRANCE
Jolivet-Reynaud, Colette, Bron, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
BIO MERIEUX, L'ETOILE, FRANCE (non-U.S. corporation)
US 2003186391 A1 20031002
APPLICATION: US 2003-430442 A1 20030507 (10)
PRIORITY: FR 1995-9643 19950803
DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 6 OF 12 USPATFULL on STN
2003:161797 Viral material and nucleotide fragments associated with multiple sclerosis, for diagnostic, prophylactic and therapeutic purposes.
Perron, Herve, Lyons, FRANCE
Beseme, Frederic, Villefontaine, FRANCE
Bedin, Frederic, Lyons, FRANCE
Paranhos-Baccala, Glaucia, Lyons, FRANCE
Komurian-Pradel, Florence, Saint Cyr Au Mont D'Or, FRANCE
Jolivet-Reynaud, Colette, Bron, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Bio Merieux, Marcy l'Etoile, FRANCE (non-U.S. corporation)
US 6579526 B1 20030617
APPLICATION: US 1999-374766 19990816 (9)
PRIORITY: FR 1995-9643 19950803
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 7 OF 12 USPATFULL on STN
2003:57100 ISOLATED NUCLEOTIDE SEQUENCES ASSOCIATED WITH MULTIPLE SCLEROSIS OR RHEUMATOID ARTHRITIS AND A PROCESS OF DETECTING.
PERRON, HERVE, LYON, FRANCE
BESEME, FREDERIC, VILLEFONTAINE, FRANCE
BEDIN, FREDERIC, LYON, FRANCE
PARANHOS-BACCALA, GLAUCIA, LYON, FRANCE
KOMURIAN-PRADEL, FLORENCE, SAINT CYR AU MONT D'OR, FRANCE
JOLIVET-REYNAUD, COLETTE, BRON, FRANCE
MANDRAND, BERNARD, VILLEURBANNE, FRANCE
GARSON, JEREMY ALEXANDER, GUILDFORD, UNITED KINGDOM
TUKE, PHILIP WILLIAM, LONDON, UNITED KINGDOM
US 2003039664 A1 20030227
APPLICATION: US 1997-979847 A1 19971126 (8)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 8 OF 12 USPATFULL on STN
2002:136578 Trypanosoma cruzi antigen, gene encoding therefore, and methods of detecting and treating chagas disease.
Paranhos-Baccala, Glaucia, Lyons, FRANCE
Lesenechal, Mylene, Villeurbanne, FRANCE
Jolivet, Michel, Bron, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Bio Merieux, Marcy l'Etoile, FRANCE (non-U.S. corporation)
US 6403103 B1 20020611
APPLICATION: US 1997-988242 19971210 (8)
PRIORITY: FR 1995-9410132 19950812
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 9 OF 12 USPATFULL on STN
2002:112312 Complex Of Lipo-Viro-Particles, Method Of Preparation And Applications.
Andre, Patrice, Lyon, FRANCE
Lotteau, Vincent, Vourles, FRANCE
Paranhos-Baccala, Glaucia, Lyon, FRANCE
Komurian-Pradel, Florence, Poleymieux, FRANCE
Bio Merieux, Marcy L' Etoile, FRANCE (non-U.S. corporation)
US 2002058044 A1 20020516
APPLICATION: US 2001-917915 A1 20010731 (9)

PRIORITY: FR 2000-10085 20000731
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 10 OF 12 USPATFULL on STN
2001:125553 Trypanosoma cruzi antigen, gene encoding therefor and methods of detecting and treating chagas disease.
Paranhos-Baccala, Glaucia, Lyons, France
Lesenechal, Mylene, Villeurbanne, France
Jolivet, Michel, Bron, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6270767 B1 20010807
APPLICATION: US 1998-138736 19980824 (9)
PRIORITY: FR 1994-10132 19940812
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 11 OF 12 USPATFULL on STN
1999:163842 Isolated nucleotide sequences associated with Multiple sclerosis.
Perron, Herve, Lyons, France
Beseme, Frederic, Villefontaine, France
Bedin, Frederic, Lyons, France
Paranhos-Baccala, Glaucia, Lyons, France
Komurian-Pradel, Florence, Saint Cyr Au Mont D'or, France
Jolivet-Reynaud, Colette, Bron, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy L'etoile, France (non-U.S. corporation)
US 6001987 19991214
APPLICATION: US 1996-691563 19960802 (8)
PRIORITY: FR 1995-9643 19950803
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L1 ANSWER 12 OF 12 USPATFULL on STN
1998:124198 Trypanosoma cruzi antigen, gene encoding therefor and methods of detecting and treating chagas disease.
Paranhos-Baccala, Glaucia, Lyons, France
Lesenechal, Mylene, Villeurbanne, France
Jolivet, Michel, Bron, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5820864 19981013
APPLICATION: US 1995-480917 19950607 (8)
PRIORITY: FR 1994-10132 19940812
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d l1,cbib,ab,clm,2-7,11

L1 ANSWER 2 OF 12 USPATFULL on STN
2004:63780 Endogeneous nucleic fragment associated with an autoimmune disease, labeling method and reagent.
Paranhos-Baccala, Glaucia, Lyon, FRANCE
Mallet, Francois, Villeurbanne, FRANCE
Voisset, Cecile, London, UNITED KINGDOM
BIO MERIEUX, MARCY L'ETOILE, FRANCE (non-U.S. corporation)
US 2004048298 A1 20040311
APPLICATION: US 2003-632793 A1 20030804 (10)
PRIORITY: FR 1999-888 19990121
DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns an endogenic nucleic fragment, such as an isolated retrovirus, integrated in the human DNA genome, the fragment being characterized in that it comprises, or consists of, at least part of the gag gene of an endogenetic retrovirus associated with an autoimmune disease or pregnancy failure or pregnancy pathologies, said part at least coding, directly and indirectly, for an expression product, or the complement of the fragment.

CLM What is claimed is:

1. Nucleic acid fragment, characterized in that it consists of at least one portion of the gag gene of an endogenous retrovirus associated with an autoimmune disease, or with unsuccessful pregnancy or pathological conditions of pregnancy, said portion being chosen from SEQ ID NO. 2 and any series of contiguous nucleotides belonging to SEQ ID NO. 2 but not belonging to SEQ ID NO. 1 and encoding an expression product, or the sequence complementary to said fragment.

2. Fragment according to claim 1, characterized in that it can be isolated from at least one of human chromosomes 1, 3, 6, 7 and 16.

3. Fragment according to claim 2, characterized in that it can be isolated from at least chromosome 3.

4. Fragment according to claim 1, characterized in that the expression product is messenger RNA.

5. Fragment according to claim 1, characterized in that the expression product is immunologically recognized by antibodies present in a biological sample from a patient suffering from an autoimmune disease.

6. Fragment according to claim 5, characterized in that the autoimmune disease is multiple sclerosis.

7. Transcription product which can be obtained by transcription of at least said portion of the gag gene of a fragment according to claim 1.

8. Method for detecting, in a biological sample, nucleotide sequences which are integrated into the DNA of the human genome and which belong to the gag gene of an endogenous retrovirus associated with an autoimmune disease, or with unsuccessful pregnancy or pathological conditions of pregnancy, characterized in that: a prior step of extraction of the cellular DNA of said biological sample is carried out, and then at least one cycle of amplification of the cellular DNA is carried out, a given probe, which hybridizes with a said nucleotide sequence and forms a hybridization complex, is brought into contact, under conditions suitable for the hybridization, with the cellular DNA present in the sample, said probe comprising at least 15 contiguous nucleotides of SEQ ID NO. 3, and the hybridization complexes formed are detected by any suitable means.

9. Method according to claim 8, characterized in that the probe is labeled with a tracer.

10. Method for detecting, in a biological sample, nucleotide sequences which are integrated into the DNA of the human genome and which belong to the gag gene of an endogenous retrovirus associated with an autoimmune disease, or with unsuccessful pregnancy or pathological conditions of pregnancy, characterized in that: a prior step of extraction of the cellular DNA of said biological sample, optionally derived from isolated chromosomes, is carried out, and then at least one

cycle of amplification of the cellular DNA is carried out, a step of in vitro transcription/translation of the amplified product is carried out, and the product derived from the transcription/translation step is reacted with a serum or plasma from a patient with an autoimmune disease.

11. Method according to claim 8, characterized in that the biological sample is a biological fluid chosen from serum, plasma, synovial fluid and urine.

12. Method for studying and/or monitoring T-cell proliferation in vitro, according to which the T cells from a patient are brought into contact with synthetic peptides belonging to SEQ ID NO. 31.

13. Method for the in situ molecular labeling of chromosomes isolated from patients, in which a probe labeled with any suitable tracer, and comprising at least 15 contiguous monomers of SEQ ID NO. 3, is used.

14. Recombinant protein obtained using an expression cassette in a bacterial host, characterized in that its protein sequence consists of SEQ ID NO. 31.

15. Protein according to claim 14, characterized in that the bacterial host is E. coli.

16. Reagent for detecting, in a biological sample, an autoimmune disease or monitoring pregnancy, comprising at least one fragment according to claim 1.

17. The method according to claim 10, wherein said endogenous retrovirus is associated with an autoimmune disease.

18. The method according to claim 17, wherein said autoimmune disease is multiple sclerosis.

19. Method according to claim 10, characterized in that the biological sample is a biological fluid chosen from serum, plasma, synovial fluid and urine.

20. Method for studying and/or monitoring T-cell proliferation in vitro, according to which the T cells from a patient are brought into contact with transcription/translation products as obtained according to the method of claim 19.

21. Reagent for detecting, in a biological sample, an autoimmune disease or monitoring pregnancy, comprising at least one transcription/translation product as obtained according to the method of claim 19.

22. Reagent for detecting, in a biological sample, an autoimmune disease or monitoring pregnancy, comprising at least one synthetic peptide belonging to SEQ ID NO: 31.

23. Reagent for detecting, in a biological sample, an autoimmune disease or monitoring pregnancy, comprising at least one protein according to claim 14.

24. A method for detecting susceptibility to an autoimmune disease or monitoring pregnancy of a patient, comprising bringing a biological sample of said patient into contact with at least one fragment according

to claim 1.

25. The method of claim 24, wherein said autoimmune disease is multiple sclerosis.

26. A method for detecting susceptibility to an autoimmune disease or monitoring pregnancy of a patient, comprising bringing a biological sample of said patient into contact with at least one transcription/translation product as obtained according to the method of claim 19.

27. The method of claim 26, wherein said autoimmune disease is multiple sclerosis.

28. A method for detecting susceptibility to an autoimmune disease or monitoring pregnancy of a patient, comprising bringing a biological sample of said patient into contact with at least one synthetic peptide belonging to SEQ ID NO: 31.

29. The method of claim 28, wherein said autoimmune disease is multiple sclerosis.

30. A method for detecting susceptibility to an autoimmune disease or monitoring pregnancy of a patient, comprising bringing a biological sample of said patient into contact with at least one protein according to claim 14.

31. The method of claim 30, wherein said autoimmune disease is multiple sclerosis.

32. The method according to claim 8, wherein said amplification is carried out by PCR using primers selected from the group consisting of SEQ I) NO: 4 to SEQ ID NO: 9 and SEQ ID NO: 12 to SEQ ID NO: 17.

33. The method according to claim 8, wherein said probe comprises at least 17 contiguous nucleotides of SEQ ID NO: 3.

34. The method according to claim 8, wherein said probe comprises at least 19 contiguous nucleotides of SEQ ID NO: 3.

35. The method according to claim 8, wherein said conditions suitable for hybridization are conditions of high stringency.

36. The method according to claim 10, wherein said amplification is carried out by PCR using primers selected from the group consisting of SEQ ID NO: 4 to SEQ ID NO: 9 and SEQ ID NO: 12 to SEQ ID NO: 17.

37. The nucleic acid fragment according to claim 1, wherein said endogenous retrovirus is associated with an autoimmune disease.

38. The nucleic acid fragment according to claim 37, wherein said autoimmune disease is multiple sclerosis.

39. The transcription product according to claim 7, wherein said endogenous retrovirus is associated with an autoimmune disease.

40. The transcription product according to claim 39, wherein said autoimmune disease is multiple sclerosis.

41. The method according to claim 8, wherein said endogenous retrovirus

is associated with an autoimmune disease.

42. The method according to claim 41, wherein said autoimmune disease is multiple sclerosis.

43. The method according to claim 9, wherein said tracer is a radioactive tracer or an enzyme.

L1 ANSWER 3 OF 12 USPATFULL on STN
2004:57379 The LTR region of MSRV-1 and the proteins it encodes and probes and methods for detecting MSRV-1 retrovirus.
Paranhos-Baccala, Glaucia, Lyon, FRANCE
Perron, Herve, Lyon, FRANCE
Komurian-Pradel, Florence, D'Or, FRANCE
Bio Merieux, Marcy L'Etoile, FRANCE, F-69280 (non-U.S. corporation)
US 2004043381 A1 20040304
APPLICATION: US 2003-637565 A1 20030811 (10)
PRIORITY: EP 1999-420041 19990215
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to a nucleotide fragment of a LTR-RU5 region comprising a nucleotide sequence which encodes the expression of a protein, wherein said protein comprises a peptide sequence selected from SEQ ID NO:2, SEQ ID NO:3 and SEQ ID NO:4, and a complementary nucleotide fragment; a probe and a primer hybridizing with said fragment; a protein encoded by said fragment; an antibody directed against said protein; and a process for detecting the presence of MSRV-1 retrovirus using a probe or an antibody of the invention.
CLM What is claimed is:
1. A nucleotide fragment of a LTR-RU5 region selected from: fragments comprising a nucleotide sequence which encodes the expression of a protein, wherein said protein comprises a peptide sequence selected from SEQ ID NO:2 and SEQ ID NO:4, fragments consisting of a nucleotide sequence which encodes the expression of a protein consisting of SEQ ID NO:3, and complementary nucleotide fragments thereof.

2. The nucleotide fragment of claim 1, wherein said protein comprises SEQ ID NO:2 and SEQ ID NO:4.

3. The nucleotide fragment of claim 1, wherein said protein consists of SEQ ID NO:2 and SEQ ID NO:4.

4. A nucleic acid probe for the detection of a LTR-RU5 region of MSRV-1 retrovirus wherein said probe comprises 10 to 1000 monomers and specifically hybridizes with a nucleotide sequence which encodes the expression of a protein, wherein said protein consists of SEQ ID NO:2, in high stringency conditions.

5. A primer for the amplification by polymerization of a nucleic acid retroviral sequence of a LTR-RU5 region of MSRV-1 virus, wherein said primer comprises 10 to 30 monomers and hybridizes with a nucleotide sequence which encodes the expression of a protein, wherein said protein consists of SEQ ID NO:2, in high stringency conditions.

6. A protein encoded by a nucleotide fragment as claimed in claim 1.

7. The protein of claim 6 comprising a peptide sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4.

8. The protein of claim 6 consisting of peptide sequence SEQ ID NO:3.

9. The protein of claim 6 comprising a peptide sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4.

10. The protein of claim 6 consisting of a peptide sequence selected from SEQ ID NO:2 and SEQ ID NO:4.

11. A polypeptide comprising at least 6 amino acids of SEQ ID NO:2.

12. Polypeptide of claim 11, comprising at least 8 amino acids of SEQ ID NO:2.

13. Polypeptide of claim 12, comprising at least 12 amino acids of SEQ ID NO:2.

14. A polyclonal or monoclonal antibody directed against a protein as claimed in claim 6.

15. A process for detecting, in a biological sample, the presence of MSRV-1 retrovirus comprising: contacting a probe of claim 4 with said biological sample, determining whether the probe binds to a nucleic acid in said biological sample, wherein binding indicates the presence of MSRV-1 virus.

16. A process for detecting, in a biological sample, the presence of MSRV-1 retrovirus comprising: contacting an antibody of claim 14 with said biological sample, determining whether the antibody binds to a protein in said biological sample, wherein binding indicates the presence of MSRV-1 virus.

17. A process for detecting, in a biological sample, the presence of MSRV-1 retrovirus comprising detecting the antigenic or biological properties of a protein as claimed in claim 6 or a fragment thereof.

18. Process of claim 17, wherein said fragment is a polypeptide comprising at least 6 amino acids of SEQ ID NO:2.

19. A polyclonal or monoclonal antibody directed against a polypeptide as claimed in claim 11.

L1 ANSWER 4 OF 12 USPATFULL on STN
2003:282306 Viral material and nucleotide fragments associated with multiple sclerosis, for diagnostic, prophylactic and therapeutic purposes.
Perron, Herve, Lyon, FRANCE
Beseme, Frederic, Villefontaine, FRANCE
Bedin, Frederic, Lyon, FRANCE
Paranhos-Baccala, Glaucia, Lyon, FRANCE
Komurian-Pradel, Florence, Saint Cyr au Mont d'Or, FRANCE
Jolivet-Reynaud, Colette, Bron, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Garson, Jeremy Alexander, Guildford, UNITED KINGDOM
Tuke, Philip William, London, UNITED KINGDOM
BIO MERIEUX, L'Etoile, FRANCE (non-U.S. corporation)
US 2003198647 A1 20031023
APPLICATION: US 2002-114104 A1 20020403 (10)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides viral material and nucleotide fragments

associated with multiple sclerosis and/or rheumatoid arthritis for use in methods of diagnosis, prophylaxis, and therapy.

CLM What is claimed is:

1. An isolated nucleic acid comprising the pol gene of a retrovirus associated with multiple sclerosis or rheumatoid arthritis.

2. The nucleic acid of claim 1, wherein said pol gene encodes a reverse transcriptase comprising an enzymatic site between amino acid domains LPQG and YXDD, wherein said virus has a phylogenetic distance from HSERV-9 of 0.063±0.1.

3. A nucleotide fragment comprising: (i) a coding nucleotide sequence selected from the group consisting of SEQ ID NO: 87, its complementary sequence, SEQ ID NO: 88, its complementary sequence, and sequences encoding the peptide sequence defined by SEQ ID NO: 89, or (ii) a portion of said coding nucleotide sequence, which encodes a peptide that is recognized by sera of patients infected with the MSRV-1 virus.

4. A process for detecting, in a biological sample, a virus associated with multiple sclerosis or rheumatoid arthritis, comprising: contacting the nucleotide fragment of claim 3 with said biological sample, and determining whether the nucleotide fragment hybridizes with a nucleic acid sequence in said biological sample, wherein hybridization indicates the presences of said virus.

5. A nucleic acid probe for the detection of a virus associated with multiple sclerosis or rheumatoid arthritis, wherein said probe specifically hybridizes with the nucleotide fragment of claim 3.

6. The probe of claim 5, consisting of between 10 and 1,000 monomers.

7. A primer for the amplification by polymerization of a nucleic acid of a viral material associated with multiple sclerosis or rheumatoid arthritis, comprising a nucleotide sequence having, for any succession of at least 20 contiguous monomers, at least 70% homology with the nucleotide sequence of the fragment of claim 3.

8. An isolated or purified polypeptide encoded by an open reading frame of the nucleotide sequence of the fragment of claim 3.

9. The polypeptide of claim 8, wherein said open reading frame comprises, in the 5' to 3' direction, the sequence between nucleotide 18 and nucleotide 2301 of SEQ ID NO: 87.

10. The polypeptide of claim 8, wherein said open reading frame is selected from the group consisting of a first open reading frame beginning at nucleotide 18 and ending at nucleotide 340 of SEQ ID NO: 87, a second open reading frame beginning at nucleotide 341 and ending at nucleotide 2304 of SEQ ID NO: 87 and a third open reading frame beginning at nucleotide 1858 and ending at nucleotide 2304 of SEQ ID NO: 87.

11. An isolated or purified polypeptide selected from the group consisting of a polypeptide comprising peptide sequence SEQ ID NO: 90, a polypeptide consisting of peptide sequence SEQ ID NO: 90, a polypeptide encoded by an open reading frame beginning at nucleotide 18 and ending at nucleotide 340 of SEQ ID NO: 87, and an equivalent polypeptide thereof which exhibits the proteolytic activity of a polypeptide of SEQ ID NO: 90.

12. An isolated or purified polypeptide selected from the group consisting of a polypeptide comprising peptide sequence SEQ ID NO: 91, a polypeptide consisting of peptide sequence SEQ ID NO: 91, a polypeptide encoded by an open reading frame beginning at nucleotide 341 and ending at nucleotide 2304 of SEQ ID NO: 87, and an equivalent polypeptide thereof which exhibits the reverse transcriptase activity of a polypeptide of SEQ ID NO: 91.

13. An isolated or purified polypeptide selected from the group consisting of a polypeptide comprising peptide sequence SEQ ID NO: 92, a polypeptide consisting of peptide sequence SEQ ID NO: 92, a polypeptide encoded by an open reading frame beginning at nucleotide 1858 and ending at nucleotide 2304 of SEQ ID NO: 87, and an equivalent polypeptide which exhibits the ribonuclease activity of a polypeptide of SEQ ID NO: 92.

14. Polypeptide of SEQ ID NO: 89.

L1 ANSWER 5 OF 12 USPATFULL on STN
2003:265376 Viral material and nucleotide fragments associated with multiple sclerosis, for diagnostic, prophylactic and therapeutic purpose.
Perron, Herve, Lyon, FRANCE
Beseme, Frederic, Villefontaine, FRANCE
Bedin, Frederic, Lyon, FRANCE
Paranhos-Baccala, Glaucia, Lyon, FRANCE
Komurian-Pradel, Florence, Saint Cyr Au Mont D'or, FRANCE
Jolivet-Reynaud, Colette, Bron, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
BIO MERIEUX, L'ETOILE, FRANCE (non-U.S. corporation)
US 2003186391 A1 20031002
APPLICATION: US 2003-430442 A1 20030507 (10)
PRIORITY: FR 1995-9643 19950803
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Viral material, in the isolated or purified state, in which the genome comprises a nucleotide sequence chosen from the group including sequences SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53 and SEQ ID NO:56, their complementary sequences and their equivalent sequences, in particular nucleotide sequences displaying, for any succession of 100 contiguous monomers, at least 50% and preferably at least 70% homology with the said sequences SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53 and SEQ ID NO:56, respectively, and their complementary sequences.
CLM What is claimed is:
1. A process for detecting a pathological and/or infective agent associated with multiple sclerosis and/or rheumatoid arthritis, in a biological sample, comprising bringing a nucleic acid into contact with the biological sample, and detecting hybridization, said nucleic acid comprising a nucleotide sequence having a succession of at least 100 contiguous monomers of a nucleotide sequence selected from the group consisting of said sequences SEQ ID NO: 46, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

2. A process for detecting a pathological and/or infective agent associated with multiple sclerosis and/or rheumatoid arthritis, in a biological sample, comprising bringing a nucleic acid into contact with the biological sample, and detecting hybridization, said nucleic acid consisting of 100 or more contiguous monomers of a nucleotide sequence selected from the group consisting of SEQ ID NO: 46, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 59,

SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

3. A process for detecting a pathological and/or infective agent associated with multiple sclerosis and/or rheumatoid arthritis, in a biological sample, comprising bringing a nucleic acid into contact with the biological sample, and detecting hybridization, said nucleic acid comprising 100 or more contiguous monomers of a nucleotide sequence selected from the group consisting of SEQ ID NO: 46, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

4. A probe for specifically hybridizing with a nucleic acid of a virus associated with multiple sclerosis, said probe comprising at least ten contiguous monomers of the nucleotide sequence of a nucleic acid, said nucleic acid comprising a nucleotide sequence having a succession of at least 100 contiguous monomers of a nucleotide sequence selected from the group consisting of SEQ ID NO: 46, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

5. A probe as defined in claim 4, having 10 to 100 contiguous monomers of said nucleotide sequence of the nucleic acid.

6. A specific primer for amplification by polymerization of a nucleic acid of a virus associated with multiple sclerosis, said primer comprising at least ten contiguous monomers of the nucleotide sequence of a nucleic acid, said nucleic acid comprising a nucleotide sequence having a succession of at least 100 contiguous monomers of a nucleotide sequence selected from the group consisting of SEQ ID NO: 46, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

7. A primer as defined in claim 6, having 10 to 100 contiguous monomers of said nucleotide sequence of the nucleic acid.

8. A process for detecting a pathological and/or infective agent associated with multiple sclerosis, in a biological sample, comprising bringing a probe according to claim 4 into contact with the biological sample, and detecting hybridization.

L1 ANSWER 6 OF 12 USPATFULL on STN
2003:161797 Viral material and nucleotide fragments associated with multiple sclerosis, for diagnostic, prophylactic and therapeutic purposes.
Perron, Herve, Lyons, FRANCE
Beseme, Frederic, Villefontaine, FRANCE
Bedin, Frederic, Lyons, FRANCE
Paranhos-Baccala, Glaucia, Lyons, FRANCE
Komurian-Pradel, Florence, Saint Cyr Au Mont D'Or, FRANCE
Jolivet-Reynaud, Colette, Bron, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Bio Merieux, Marcy l'Etoile, FRANCE (non-U.S. corporation)
US 6579526 B1 20030617
APPLICATION: US 1999-374766 19990816 (9)
PRIORITY: FR 1995-9643 19950803
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Viral material, in the isolated or purified state, in which the genome comprises a nucleotide sequence chosen from the group including sequences SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53 and SEQ ID NO:56, their complementary sequences and their equivalent sequences, in particular nucleotide sequences displaying, for any succession of 100 contiguous monomers, at least 50% and preferably at least 70% homology with the said sequences SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53 and SEQ ID NO:56, respectively, and their complementary sequences.

CLM What is claimed is:

1. An isolated nucleic acid comprising a nucleotide sequence having a succession of at least 100 contiguous monomers of a nucleotide sequence selected from the group consisting of sequences SEQ ID NO: 46, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

2. A nucleic acid according to claim 1, wherein said nucleotide sequence is selected from the group consisting of sequences SEQ ID NO: 51, SEQ ID NO: 56, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89, their complementary sequences and nucleotide sequences having a succession of at least 100 contiguous monomers of a nucleotide sequence selected from the group consisting of said sequences SEQ ID NO: 51, SEQ ID NO: 56, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

3. An isolated nucleic acid consisting of 100 or more contiguous monomers of a nucleotide sequence selected from the group consisting of SEQ ID NO: 46, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

4. A nucleic acid according to claim 3, consisting of a nucleotide sequence selected from the group consisting of SEQ ID NO: 46, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

5. A nucleic acid according to claim 3, consisting of 100 or more contiguous monomers of a nucleotide sequence selected from the group consisting of SEQ ID NO: 51, SEQ ID NO: 56, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

6. A nucleic acid according to claim 3, consisting of a nucleotide sequence selected from the group consisting of SEQ ID NO: 51, SEQ ID NO: 56, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

7. An isolated nucleic acid comprising 100 or more contiguous monomers of a nucleotide sequence selected from the group consisting of SEQ ID NO: 46, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 56, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

8. A nucleic acid according to claim 7, wherein said nucleotide sequence is selected from the group consisting of SEQ ID NO: 51, SEQ ID NO: 56, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 89 and their complementary sequences.

L1 ANSWER 7 OF 12 USPATFULL on STN

2003:57100 ISOLATED NUCLEOTIDE SEQUENCES ASSOCIATED WITH MULTIPLE SCLEROSIS OR RHEUMATOID ARTHRITIS AND A PROCESS OF DETECTING.

PERRON, HERVE, LYON, FRANCE
BESEME, FREDERIC, VILLEFONTAINE, FRANCE
BEDIN, FREDERIC, LYON, FRANCE
PARANHOS-BACCALA, GLAUCIA, LYON, FRANCE
KOMURIAN-PRADEL, FLORENCE, SAINT CYR AU MONT D'OR, FRANCE
JOLIVET-REYNAUD, COLETTE, BRON, FRANCE
MANDRAND, BERNARD, VILLEURBANNE, FRANCE
GARSON, JEREMY ALEXANDER, GUILDFORD, UNITED KINGDOM
TUKE, PHILIP WILLIAM, LONDON, UNITED KINGDOM

US 2003039664 A1 20030227
APPLICATION: US 1997-979847 A1 19971126 (8)
DOCUMENT TYPE: Utility; APPLICATION.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides viral material and nucleotide fragments associated with multiple sclerosis and/or rheumatoid arthritis for use in methods of diagnosis, prophylaxis, and therapy.

CLM What is claimed is:

1. An isolated or purified nucleic acid, comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:93, SEQ ID NO:94, their complementary sequences, and their equivalent sequences, excluding HSERV-9 sequences.

2. The nucleic acid of claim 1, wherein said nucleotide sequence is selected from the group consisting of SEQ ID NO:93, its complementary sequence, and their equivalent sequences.

3. The nucleic acid of claim 1, wherein said nucleotide sequence is selected from the group consisting of SEQ ID NO:94, its complementary sequence, and their equivalent sequences.

4. The nucleic acid of claim 1, wherein said equivalent sequences display, for any succession of 100 contiguous monomers, at least 80% homology with said SEQ ID NO:93 or its complementary sequence.

5. An isolated or purified nucleic acid coding for a polypeptide displaying, for any contiguous succession of at least 30 amino acids, at least 70% homology with a peptide sequence encoded by SEQ ID NO:93, SEQ ID NO:94, or their complementary sequences.

6. An isolated or purified retroviral nucleic acid, comprising the pol gene of an isolated retrovirus associated with multiple sclerosis or rheumatoid arthritis, or its equivalent sequences.

7. The nucleic acid of claim 6, wherein said equivalent sequences are 80% homologous to said pol gene.

8. A nucleic acid comprising the pol gene of an isolated virus encoding a reverse transcriptase comprising an enzymatic site between amino acid domains LPQG and YXDD, wherein said virus has a phylogenetic distance from HSERV-9 of 0.063±0.1, or its equivalent sequences.

9. A nucleotide fragment comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:93, SEQ ID NO:94, their complementary sequences, and their equivalent sequences, wherein said group excludes SEQ ID NO:1, and wherein said nucleotide fragment does not comprise the sequence HSERV-9.

10. The nucleotide fragment of claim 9, wherein said equivalent

sequences display, for any succession of 100 contiguous monomers, at least 80% homology with SEQ ID NO:93, SEQ ID NO:94, or their complementary sequences.

11. A process for detecting, in a biological sample, a virus associated with multiple sclerosis or rheumatoid arthritis, comprising: contacting the nucleotide fragment of claim 9, with said biological sample, determining whether the nucleotide fragment hybridizes with a nucleic acid in said biological sample, wherein hybridization indicates the presence of said virus.

12. A nucleotide fragment comprising a coding nucleotide sequence, its equivalent sequence, or a portion thereof, wherein said nucleotide sequence is selected from the group consisting of: SEQ ID NO:93, its complementary sequence; SEQ ID NO:94, its complementary sequence; and sequences encoding the peptide sequence defined by SEQ ID NO:95, wherein said coding nucleotide sequence, equivalent sequence, or portion thereof, encodes a peptide that is recognized by sera of patients infected with the MSRV-1 virus, and/or in whom the MSRV-1 virus has been reactivated.

13. A process for detecting, in a biological sample, a virus associated with multiple sclerosis or rheumatoid arthritis, comprising: contacting the nucleotide fragment of claim 12 with said biological sample, determining whether the nucleotide fragment hybridizes with a nucleic acid in said biological sample, wherein hybridization indicates the presence of said virus.

14. An isolated or purified nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:169 to SEQ ID NO:172 and SEQ ID NO:176 to SEQ ID NO:179, their complementary sequences, and their equivalent sequences, excluding HSERV-9 sequence.

15. The nucleic acid of claim 14, wherein said equivalent sequences display, for any succession of 100 contiguous monomers, at least 70% homology with said SEQ ID NO:169 to SEQ ID NO:172 and SEQ ID NO:176 to SEQ ID NO:179, or their complementary sequences.

16. The nucleic acid of claim 15, wherein said equivalent sequences display, for any succession of 100 contiguous monomers, at least 80% homology with said SEQ ID NO:169 to SEQ ID NO:172 and SEQ ID NO:176 to SEQ ID NO:179, or their complementary sequences.

17. An isolated or purified nucleic acid coding for a polypeptide displaying, for any contiguous succession of at least 30 amino acids, at least 70% homology with a peptide sequence encoded by SEQ ID NO:169 to SEQ ID NO:172 and SEQ ID NO:176 to SEQ ID NO:179, or their complementary sequences.

18. A nucleotide fragment comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:169 to SEQ ID NO:172 and SEQ ID NO:176 to SEQ ID NO:179, their complementary sequences, and their equivalent sequences, wherein said group excludes SEQ ID NO:1, and wherein said nucleotide fragment does not comprise the sequence HSERV-9.

19. The nucleotide fragment of claim 18, wherein said equivalent sequences display, for any succession of 100 contiguous monomers, at least 70% homology with SEQ ID NO:169 to SEQ ID NO:172 and SEQ ID NO:176 to SEQ ID NO:179, or their complementary sequences.

20. The nucleotide fragment of claim 18, wherein said equivalent sequences display, for any succession of 100 contiguous monomers, at least 80% homology with SEQ ID NO:169 to SEQ ID NO:172 and SEQ ID NO:176 to SEQ ID NO:179, or their complementary sequences.

21. A process for detecting, in a biological sample, a virus associated with multiple sclerosis or rheumatoid arthritis, comprising: contacting the nucleotide fragment of claim 18 with said biological sample, determining whether the nucleotide fragment hybridizes with a nucleic acid in said biological sample, wherein hybridization indicates the presence of said virus.

22. A nucleotide fragment comprising a coding nucleotide sequence, its equivalent sequence, or a portion thereof, wherein said nucleotide sequence is selected from the group consisting of: SEQ ID NO:169 to SEQ ID NO:172 and their complementary sequences; and sequences encoding the peptide sequence defined by SEQ ID NO:173 to SEQ ID NO:175, wherein said coding nucleotide sequence, equivalent sequence, or portion thereof, encodes a peptide that is recognized by sera of patients infected with the MSRV-1 virus, and/or in whom the MSRV-1 virus has been reactivated.

23. A process for detecting, in a biological sample, a virus associated with multiple sclerosis or rheumatoid arthritis, comprising: contacting the nucleotide fragment of claim 22 with said biological sample, determining whether the nucleotide fragment hybridizes with a nucleic acid in said biological sample, wherein hybridization indicates the presence of said virus.

24. A nucleotide fragment comprising a coding nucleotide sequence, its equivalent sequence, or a portion thereof, wherein said nucleotide sequence is selected from the group consisting of: SEQ ID NO:176 to SEQ ID NO:179, and their complementary sequences; and sequences encoding the peptide sequence defined by SEQ ID NO:180 to SEQ ID NO:182, wherein said coding nucleotide sequence, equivalent sequence, or portion thereof, encodes a peptide that is recognized by sera of patients infected with the MSRV-1 virus, and/or in whom the MSRV-1 virus has been reactivated.

25. A nucleic acid probe for the detection of a virus associated with multiple sclerosis or rheumatoid arthritis, wherein said probe specifically hybridizes with the nucleotide sequence of the nucleotide fragment of claim 9.

26. A nucleic acid probe for the detection of a virus associated with multiple sclerosis or rheumatoid arthritis, wherein said probe specifically hybridizes with the nucleotide fragment of claim 12.

27. The probe of claim 25, consisting of between 10 and 1,000 monomers.

28. The probe of claim 26, consisting of between 10 and 1,000 monomers.

29. A primer for the amplification by polymerization of a nucleic acid of a viral material associated with multiple sclerosis or rheumatoid arthritis, comprising a nucleotide sequence having, for any succession of at least 20 contiguous monomers, at least 70% homology with the nucleotide sequence of the fragment of claim 9.

30. A primer for the amplification by polymerization of a nucleic acid of a viral material associated with multiple sclerosis or rheumatoid

arthritis, comprising a nucleotide sequence having, for any succession of at least 20 contiguous monomers, at least 70% homology with the nucleotide sequence of the fragment of claim 12.

31. The primer of claim 29, comprising a sequence selected from the group consisting of SEQ ID NO:99 to SEQ ID NO:111.

32. A nucleic acid probe for the detection of a virus associated with multiple sclerosis or rheumatoid arthritis, wherein said probe specifically hybridizes with the nucleotide sequence of the fragment of claim 18.

33. A nucleic acid probe for the detection of a virus associated with multiple sclerosis or rheumatoid arthritis, wherein said probe specifically hybridizes with the nucleotide sequence of the fragment of claim 22.

34. A nucleic acid probe for the detection of a virus associated with multiple sclerosis or rheumatoid arthritis, wherein said probe specifically hybridizes with the nucleotide sequence of the fragment of claim 24.

35. The probe of claim 32, consisting of between 10 and 1,000 monomers.

36. The probe of claim 33, consisting of between 10 and 1,000 monomers.

37. The probe of claim 34, consisting of between 10 and 1,000 monomers.

38. A primer for the amplification by polymerization of a nucleic acid of a viral material associated with multiple sclerosis or rheumatoid arthritis, comprising a nucleotide sequence having, for any succession of at least 20 contiguous monomers, at least 70% homology with the nucleotide sequence of the fragment of claim 18.

39. A primer for the amplification by polymerization of a nucleic acid of a viral material associated with multiple sclerosis or rheumatoid arthritis, comprising a nucleotide sequence having, for any succession of at least 20 contiguous monomers, at least 70% homology with the nucleotide sequence of the fragment of claim 22.

40. A primer for the amplification by polymerization of a nucleic acid of a viral material associated with multiple sclerosis or rheumatoid arthritis, comprising a nucleotide sequence having, for any succession of at least 20 contiguous monomers, at least 70% homology with the nucleotide sequence of the fragment of claim 24.

41. The primer of claim 39, comprising a sequence selected from the group consisting of SEQ ID NO:183 to SEQ ID NO:186.

42. An isolated or purified polypeptide encoded by an open reading frame of the nucleotide sequence of the fragment of claim 9.

43. An isolated or purified polypeptide encoded by an open reading frame of the nucleotide sequence of the fragment of claim 12.

44. The polypeptide of claim 42, wherein said open reading frame comprises, in the 5' to 3' direction, the sequence between nucleotide 18 and nucleotide 2304 of SEQ ID NO:93.

45. An isolated or purified polypeptide comprising the peptide sequence

of SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, or their equivalent sequences.

46. The polypeptide of claim 45, comprising the peptide sequence of SEQ ID NO:95, or its equivalent sequences.

47. The polypeptide of claim 45, comprising the peptide sequence of SEQ ID NO:96, or its equivalent sequences.

48. The polypeptide of claim 47, wherein said polypeptide exhibits proteolytic activity.

49. A polypeptide encoded by an open reading frame selected from the group consisting of a first open reading frame beginning at nucleotide 18 and ending at nucleotide 340 of SEQ ID NO:93, a second open reading frame beginning at nucleotide 341 and ending at nucleotide 2304 of SEQ ID NO:93, and a third open reading frame, beginning at nucleotide 1858 and ending at nucleotide 2304 of SEQ ID NO:93.

50. The polypeptide of claim 49, wherein said open reading frame begins at nucleotide 18 and ends at nucleotide 340 of SEQ ID NO:93.

51. A polypeptide exhibiting an inhibitory activity on the proteolytic activity of polypeptide of claim 48.

52. The polypeptide of claim 45, comprising the peptide sequence of SEQ ID NO:97, or its equivalent sequences.

53. The polypeptide of claim 52, further comprising the peptide sequence of SEQ ID NO:98 or its equivalent sequences.

54. The polypeptide of claim 49, wherein said open reading frame begins at nucleotide 341 and ends at nucleotide 2304 of SEQ ID NO:93.

55. The polypeptide of claim 49, wherein said open reading frame begins at nucleotide 1858 and ends at nucleotide 2304 of SEQ ID NO:93.

56. The polypeptide of claim 52, wherein said polypeptide exhibits a reverse transcriptase activity.

57. The polypeptide of claim 54, wherein said polypeptide exhibits a reverse transcriptase activity.

58. The polypeptide of claim 53, wherein said polypeptide exhibits a ribonuclease H activity.

59. The polypeptide of claim 55, wherein said polypeptide exhibits a ribonuclease H activity.

60. A polypeptide having an inhibitory activity on the reverse transcriptase activity of the polypeptide of claim 56.

61. A polypeptide having an inhibitory activity on the ribonuclease H activity of the polypeptide of claim 58.

62. An isolated or purified antigenic polypeptide having a peptide sequence selected from the group consisting of SEQ ID NO:95, its equivalent sequences, and fragments thereof, wherein said polypeptide is recognized by the sera of patients infected with the MSRV-1 virus, and/or in whom the MSRV-1 virus has been reactivated.

63. The polypeptide of claim 62, wherein said fragment is selected from the group consisting of SEQ ID NO:96, SEQ ID NO:97, and SEQ ID NO:98.

64. A process for detecting, in a biological sample, the presence of, or exposure to, a virus associated with multiple sclerosis or rheumatoid arthritis, comprising: contacting the polypeptide of claim 42 with said biological sample, determining whether the polypeptide binds with a peptide in said biological sample, wherein binding indicates the presence of or exposure to said virus.

65. An isolated or purified polypeptide encoded by an open reading frame of the nucleotide sequence of the fragment of claim 18.

66. An isolated or purified polypeptide encoded by an open reading frame of the nucleotide sequence of the fragment of claim 22.

67. An isolated or purified polypeptide encoded by an open reading frame of the nucleotide sequence of the fragment of claim 24.

68. An isolated or purified polypeptide comprising a peptide sequence selected from the group consisting of SEQ ID NO:173 to SEQ ID NO:175, SEQ ID NO:180 to SEQ ID NO:182, and their equivalent sequences.

69. An isolated or purified antigenic polypeptide having a peptide sequence selected from the group consisting of SEQ ID NO:173 to SEQ ID NO:175, SEQ ID NO:180 to SEQ ID NO:182, their equivalent sequences, and fragments thereof, wherein said polypeptide is recognized by the sera of patients infected with the MSRV-1 virus, and/or in whom the MSRV-1 virus has been reactivated.

70. The polypeptide of claim 69, wherein said fragment is selected from the group consisting of SEQ ID NO:173 to SEQ ID NO:175 and SEQ ID NO:180 to SEQ ID NO:182.

71. A process for detecting, in a biological sample, the presence of, or exposure to, a virus associated with multiple sclerosis or rheumatoid arthritis, comprising: contacting the polypeptide of claim 65 with said biological sample, and determining whether the polypeptide binds to a peptide in said biological sample, wherein binding indicates the presence of, or exposure to, said virus.

72. An antibody directed against the MSRV-1 virus, said antibody being obtained by immunologically reacting a human or animal body or cells with an immunogenic agent consisting of the antigenic polypeptide of claim 62.

73. A process for detecting, in a biological sample, the presence of, or exposure to, a virus associated with multiple sclerosis or rheumatoid arthritis, comprising: contacting the antibody of claim 72 with said biological sample, determining whether the antibody binds to a peptide in said biological sample, wherein antibody binding indicates the presence of, or exposure to, said virus.

74. An antibody directed against the MSRV-1 virus, wherein said antibody is obtained by immunologically reacting a human or animal body or cells with an immunogenic agent consisting of the antigenic polypeptide of claim 69.

75. A process for detecting, in a biological sample, the presence of, or

exposure to, a virus associated with multiple sclerosis or rheumatoid arthritis, comprising: contacting the antibody of claim 74 with said biological sample, and determining whether the antibody binds to a peptide in said biological sample, wherein antibody binding indicates the presence of, or exposure to, said virus.

L1 ANSWER 11 OF 12 USPATFULL on STN
1999:163842 Isolated nucleotide sequences associated with Multiple sclerosis.
Perron, Herve, Lyons, France
Beseme, Frederic, Villefontaine, France
Bedin, Frederic, Lyons, France
Paranhos-Baccala, Glaucia, Lyons, France
Komurian-Pradel, Florence, Saint Cyr Au Mont D'or, France
Jolivet-Reynaud, Colette, Bron, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy L'etoile, France (non-U.S. corporation)
US 6001987 19991214
APPLICATION: US 1996-691563 19960802 (8)
PRIORITY: FR 1995-9643 19950803
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Viral material, in the isolated or purified state, in which the genome comprises a nucleotide sequence chosen from the group including sequences SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53 and SEQ ID NO:56, their complementary sequences and their equivalent sequences, in particular nucleotide sequences displaying, for any succession of 100 contiguous monomers, at least 50% and preferably at least 70% homology with the said sequences SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53 and SEQ ID NO:56, respectively, and their complementary sequences.
CLM What is claimed is:
1. An isolated, purified or synthesized nucleotide sequence comprising a sequence selected from the group consisting of: SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:89, and a complementary sequence complementary to one of said SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61 or SEQ ID NO:89.

```
=> e perron herve/in
E1            1     PERRON GILBERT/IN
E2            1     PERRON HENRI/IN
E3           22 --> PERRON HERVE/IN
E4            1     PERRON III MARIUS R/IN
E5            6     PERRON JAMES S/IN
E6            3     PERRON JEAN/IN
E7            1     PERRON JEAN NOEL/IN
E8            1     PERRON JEAN PIERRE/IN
E9            1     PERRON JEROME C/IN
E10           2     PERRON JOCELYN/IN
E11           2     PERRON JOSEPH/IN
E12           1     PERRON JOSEPH M/IN

=> s e3
L2           22 "PERRON HERVE"/IN

=> s l2 not l1
L3           16 L2 NOT L1
```

=> d l3,cbib,1-16

L3 ANSWER 1 OF 16 USPATFULL on STN
2004:227928 Endogenetic retroviral sequences, associated with autoimmune diseases or with pregnancy disorders.
Beseme, Frederic, Villefontaine, FRANCE
Blond, Jean-Luc, Lyon, FRANCE
Bouton, Olivier, Francheville, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Mallet, Francois, Villeurbanne, FRANCE
Perron, Herve, Lyon, FRANCE
BIO MERIEUX, Marcy L'Etoile, FRANCE (non-U.S. corporation)
US 2004176314 A1 20040909
APPLICATION: US 2003-717580 A1 20031121 (10)
PRIORITY: FR 1997-8815 19970707
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 2 OF 16 USPATFULL on STN
2003:115580 Polypeptide capable of reacting with antibodies of patients suffering from multiple sclerosis and uses.
Jolivet-Reynaud, Colette, Bron, FRANCE
Perron, Herve, Lyons, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Bio Merieux, Marcy l'Etoile, FRANCE (non-U.S. corporation)
US 6555091 B1 20030429
WO 9849285 19981105
APPLICATION: US 1999-403343 19991018 (9)
WO 1998-FR870 19980429
PRIORITY: FR 1997-5679 19970429
FR 1997-16870 19971231
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 3 OF 16 USPATFULL on STN
2002:19207 Cell lines and viral isolates associated with multiple sclerosis.
Perron, Herve, Grenoble, FRANCE
Mallet, Francois, Villeurbanne, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Bedin, Frederic, Lyons, FRANCE
Beseme, Frederic, Villefontaine, FRANCE
Bio Merieux, Marcy l'Etoile, FRANCE (non-U.S. corporation)
US 6342383 B1 20020129
APPLICATION: US 1998-133411 19980813 (9)
PRIORITY: FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-1529 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 4 OF 16 USPATFULL on STN
2001:158057 Process and culture medium for the production of cells infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)

US 6291225 B1 20010918
APPLICATION: US 1995-485145 19950607 (8)
PRIORITY: FR 1992-4322 19920403
FR 1992-13443 19921103
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 5 OF 16 USPATFULL on STN
2001:125726 Method for detecting and/or quantifying a gliotoxic factor.
Malcus-Vocanson, Carine, Brignais, France
Perron, Herve, Lyons, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6270953 B1 20010807
WO 9811439 19980319
APPLICATION: US 1999-202118 19990329 (9)
WO 1997-FR1620 19970912 19990329 PCT 371 date 19990329 PCT 102(e) date
PRIORITY: FR 1996-11347 19960912
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 6 OF 16 USPATFULL on STN
2001:18272 Viral isolates associated with multiple sclerosis.
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyon, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6184025 B1 20010206
APPLICATION: US 1998-200990 19981130 (9)
PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 7 OF 16 USPATFULL on STN
2000:70666 Process and culture medium for the production of cells infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6071736 20000606
APPLICATION: US 1996-754010 19961120 (8)
PRIORITY: FR 1992-13443 19921103
FR 1993-9204322 19930403
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 8 OF 16 USPATFULL on STN
1999:121120 MSRV1 virus and MSRV2 pathogen and/or infective agent associated with multiple sclerosis, and biopolymer constituents thereof.
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France

Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy I'Etoile, France (non-U.S. corporation)
US 5962217 19991005
APPLICATION: US 1995-470006 19950606 (8)
PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 9 OF 16 USPATFULL on STN
1999:81747 Process for the production of a viable cell culture infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, L'Etoile, France (non-U.S. corporation)Universite Joseph Fourier (Grenoble 1), Grenoble Cedex, France (non-U.S. corporation)
US 5925555 19990720
APPLICATION: US 1996-651573 19960522 (8)
PRIORITY: FR 1992-4322 19920403
FR 1992-13447 19921103
DOCUMENT TYPE: Utility; Granted.

L3 ANSWER 10 OF 16 USPATFULL on STN
1999:27417 Cytotoxic factor as is associated with multiple sclerosis, its detection and its quantification.
Perron, Herve, Grenoble, France
Dobransky, Tomas, Marly-le-Roy, France
Rieger, Fran.cedilla.ois, Paris, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5876954 19990302
APPLICATION: US 1995-389164 19950215 (8)
PRIORITY: FR 1994-1946 19940215
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 11 OF 16 USPATFULL on STN
1999:21977 Retrovirus agents MSRV1 and MSRV2 associated with multiple sclerosis
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5871996 19990216
APPLICATION: US 1995-384137 19950206 (8)
PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 12 OF 16 USPATFULL on STN
1999:21732 Multiple sclerosis related virus.
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 5871745 19990216
APPLICATION: US 1995-471969 19950606 (8)
PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 13 OF 16 USPATFULL on STN
1998:104553 Detection of MSRV1 virus and MSRV2 pathogen and/or infective agent associated with multiple sclerosis, by nucleic acid hybridization.
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5800980 19980901
APPLICATION: US 1995-471724 19950606 (8)
PRIORITY: FR 1999-9401529 18990204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 14 OF 16 USPATFULL on STN
1998:27921 Cytotoxic factor as is associated with multiple sclerosis, its detection and its quantification.
Perron, Herve, Grenoble, France
Dobransky, Tomas, Marly-Le-Roy, France
Rieger, Fran.cedilla.ois, Paris, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy L'etoile, France (non-U.S. corporation)
US 5728540 19980317
APPLICATION: US 1995-468670 19950606 (8)
PRIORITY: FR 1994-1946 19940215
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 15 OF 16 USPATFULL on STN
97:63920 Process and culture medium for the production of cells infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy l' Etoile, France (non-U.S. corporation)
US 5650318 19970722

WO 9320188 19931014
APPLICATION: US 1994-157061 19940202 (8)
WO 1993-FR336 19930402 19940202 PCT 371 date 19940202 PCT 102(e) date
PRIORITY: FR 1992-4322 19920403
FR 1992-13443 19921103
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 16 OF 16 USPATFULL on STN
96:116271 Process for the production of a viable cell culture infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)Universite Joseph Fourier, Grenoble, France (non-U.S. corporation)
US 5585262 19961217
WO 9320189 19931014
APPLICATION: US 1994-157060 19940202 (8)
WO 1993-FR337 19930402 19940202 PCT 371 date 19940202 PCT 102(e) date
PRIORITY: FR 1992-4322 19920403
FR 1992-13447 19921103
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d l3,cbib,ab,clm,1-16

L3 ANSWER 1 OF 16 USPATFULL on STN
2004:227928 Endogenetic retroviral sequences, associated with autoimmune diseases or with pregnancy disorders.
Beseme, Frederic, Villefontaine, FRANCE
Blond, Jean-Luc, Lyon, FRANCE
Bouton, Olivier, Francheville, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Mallet, Francois, Villeurbanne, FRANCE
Perron, Herve, Lyon, FRANCE
BIO MERIEUX, Marcy L'Etoile, FRANCE (non-U.S. corporation)
US 2004176314 A1 20040909
APPLICATION: US 2003-717580 A1 20031121 (10)
PRIORITY: FR 1997-8815 19970707
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns a genomic retroviral nucleic material, in an isolated or purified state, at least partially functional or non-functional, wherein the genome comprises a reference nucleotide sequence selected from the group including sequences of SEQ ID NOs: 1-15, their complementary sequences, and their equivalent sequences, in particular, nucleotide sequences having, for every series of 100 contiguous monomers, at least 70% and preferably at least 90% homology with the sequences of SEQ ID NOs: 1-15. The invention also concerns the application of this material.
CLM What is claimed is:
1. A nucleic material, in an isolated or purified state, comprising a nucleotide sequence selected from the group consisting of sequences of SEQ ID NOs: 1 to 15, their complementary sequences, and sequences that exhibit for every sequence of 100 contiguous monomers at least 70% homology with said sequences of SEQ ID NOs: 1 to 15, respectively.

2. A nucleic material, in an isolated or purified state, comprising a nucleotide sequence, encoding any polypeptide exhibiting, for every

contiguous sequence of at least 30 amino acids, at least 80% identity with a peptide sequence encoded by at least a functional part of a nucleotide sequence selected from the group consisting of sequences of SEQ ID NOs: 1 to 15 and their complementary sequences.

3. The nucleic material according to claim 1, comprising a nucleic fragment inserted between two sequences corresponding respectively to the LTR region and to the gag gene for a retroviral genomic structure.

4. A nucleic material consisting of a nucleotide sequence identical to SEQ ID NO: 11, with at least one deletion.

5. A nucleic material according to claim 1, comprising at least one functional nucleotide sequence encoding at least one retroviral protein.

6. A nucleic material according to claim 1, comprising at least one regulatory nucleotide sequence.

7. A nucleotide fragment comprising a nucleotide sequence selected from the group consisting of: (a) a nucleotide sequence of at least 100 bases of a clone selected from the group consisting of: cl.6A2 (SEQ ID NO: 1), cl.6A1 (SEQ ID NO: 2), cl.7A16 (SEQ ID NO: 3), cl.Pi22 (SEQ ID NO: 4), cl.24.4 (SEQ ID NO: 5), cl.C4C5 (SEQ ID NO: 6), cl.PH74 (SEQ ID NO: 7), cl.PH7 (SEQ ID NO: 8), cl.Pi5T (SEQ ID NO: 9), cl.44.4 (SEQ ID NO: 10), HERV-W (SEQ ID NO: 11), cl.6A5 (SEQ ID NO: 12), cl.7A20 (SEQ ID NO: 13), cl.7A21 (SEQ ID NO: 14), and LTR (SEQ ID NO: 15); (b) sequences which are respectively complementary to the sequences according to (a); and (c) equivalent sequences which have respectively at least 50% homology to the sequences according to (a) and (b).

8. A nucleic probe for the detection of a nucleic material, wherein said nucleic probe hybridizes under highly stringent conditions with the nucleotide sequence of the nucleic material according to claim 1.

9. A probe according to claim 8, comprising a label.

10. A nucleic primer for the amplification by polymerization of an RNA or of a DNA, comprising a nucleotide sequence that hybridizes under highly stringent conditions with the nucleotide sequence of the nucleic material according to claim 1.

11. A nucleic probe or nucleic primer, comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 16 to 28.

12. An RNA or DNA, comprising a nucleotide fragment according to claim 7.

13. The nucleic probe according to claim 8, wherein said probe contains at least 6 monomers.

14. The nucleic probe according to claim 13, wherein said probe contains no more than 100 monomers.

15. The nucleic probe according to claim 13, wherein said probe contains at least 6 contiguous monomers of a sequence selected from the group consisting of SEQ ID NOs: 1-15 and their complementary sequences.

16. The nucleic probe according to claim 8, wherein said probe has at least 70% homology with a sequence selected from the group consisting of

SEQ ID NOs: 1-15 and their complementary sequences.

17. The nucleic probe according to claim 16, wherein said probe has at least 90% homology with a sequence selected from the group consisting of SEQ ID NOs: 1-15 and their complementary sequences.

18. A method for the molecular labeling of at least one member selected from the group consisting of an autoimmune disease, a pathology associated with an autoimmune disease, a pathological pregnancy, and an unsuccessful pregnancy, said method comprising: at least one of identifying and quantifying any nucleotide fragment according to claim 7 in any biological body material.

19. The method according to claim 18, further comprising: detecting cells expressing the nucleotide fragment in said biological body material.

20. A diagnostic composition comprising a nucleic material according to claim 1.

21. A method of diagnosing an autoimmune disease, a pathology associated with an autoimmune disease, a pathological pregnancy, or an unsuccessful pregnancy, said method comprising: obtaining a biological sample; contacting said biological sample with a molecular marker comprising a nucleic material according to claim 1; and detecting for said molecular marker.

22. A method of diagnosing susceptibility to an autoimmune disease or a pathology associated with an autoimmune disease, a risk of a pathological pregnancy, or a risk of an unsuccessful pregnancy, said method comprising: obtaining a biological sample; contacting said biological sample with a chromosomal marker comprising a nucleic material according to claim 1; and detecting for said chromosomal marker.

23. A method of detecting a gene associated with susceptibility to an autoimmune disease or a pathology associated with an autoimmune disease, a risk of a pathological pregnancy, or a risk of an unsuccessful pregnancy, said method comprising: obtaining a biological sample; contacting said biological sample with a proximity marker comprising a nucleic material according to claim 1; and detecting for said proximity marker.

24. The method of claim 18, wherein said biological body material comprises a body fluid.

25. The nucleic material according to claim 1, wherein said nucleotide sequence exhibits, for every sequence of 100 contiguous monomers, at least 90% homology with said sequences of SEQ ID NOs: 1 to 15, respectively.

26. The nucleic material according to claim 2, wherein said polypeptide exhibits, for every contiguous sequence of at least 30 amino acids, at least 90% identity with a peptide sequence capable of being encoded by at least a functional part of said nucleotide sequence selected from the group consisting of sequences of SEQ ID NOs: 1-15 and their complementary sequences.

27. The nucleic material of the retroviral genomic type according to claim 2, comprising a nucleic fragment inserted between two sequences

corresponding respectively to the LTR region and to the gag gene for said retroviral genomic structure.

28. The nucleic material according to claim 27, wherein said nucleic fragment comprises the sequence of SEQ ID NO: 12.

29. The nucleic material according to claim 3, wherein said nucleic fragment comprises the sequence of SEQ ID NO: 12.

30. The nucleic material according to claim 4, wherein said nucleotide sequence comprises a sequence selected from the group consisting of the sequences of SEQ ID NOs: 7, 8 and 9.

31. The nucleic material according to claim 4, comprising at least one functional nucleotide sequence encoding at least one retroviral protein.

32. The nucleic material according to claim 4, comprising at least one regulatory nucleotide sequence.

33. A replication vector, comprising a nucleotide fragment according to claim 7.

34. A nucleotide fragment according to claim 7, wherein said equivalent sequences exhibit at least 70% homology with the sequences according to (a) and (b).

35. A nucleotide fragment according to claim 7, wherein said equivalent sequences exhibit at least 90% homology with the sequences according to (a) and (b).

L3 ANSWER 2 OF 16 USPATFULL on STN
2003:115580 Polypeptide capable of reacting with antibodies of patients suffering from multiple sclerosis and uses.
Jolivet-Reynaud, Colette, Bron, FRANCE
Perron, Herve, Lyons, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Bio Merieux, Marcy l'Etoile, FRANCE (non-U.S. corporation)
US 6555091 B1 20030429
WO 9849285 19981105
APPLICATION: US 1999-403343 19991018 (9)
WO 1998-FR870 19980429
PRIORITY: FR 1997-5679 19970429
FR 1997-16870 19971231
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns a polypeptide specifically reacting with the antibodies of patients suffering from multiple sclerosis (SEP) and whereof the peptide sequence comprises at least one sequence selected among SEQ ID No. 1 to SEQ ID NO: 19, and their equivalent sequences, and the use of this polypeptide in a reagent and a kit for detecting multiple sclerosis, an immunoreactive composition and in a method for fixing, in a biological sample, antibodies characteristic and/or specific of multiple sclerosis.
CLM What is claimed is:
1. Polypeptide capable of reacting specifically with the antibodies of patients suffering from multiple sclerosis (MS) and whose peptide sequence comprises at least one sequence chosen from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 12 to SEQ ID NO: 14, SEQ ID NO: 16 and SEQ ID NO: 19, said polypeptide having no more than 20

amino acids.

2. Polypeptide of claim 1, said polypeptide having no more than 15 amino acids.

3. Reagent for the detection of multiple sclerosis in a patient and/or the monitoring of a patient suffering from multiple sclerosis, characterized in that it comprises at least one polypeptide according to claim 1, said polypeptide being optionally labeled.

4. Reagent according to claim 3, characterized in that it comprises at least two different polypeptides.

5. Polynucleotide whose nucleotide sequence encodes a polypeptide according to claim 1.

6. Polypeptide capable of reacting with the antibodies of patients suffering from multiple sclerosis (MS) and whose peptide sequence consists of a sequence selected from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 12 to SEQ ID NO: 14, SEQ ID NO: 16 and SEQ ID NO: 19.

7. Polypeptide capable of reacting with at least one antibody in at least one biological fluid from a patient in whom the MSRV-1 viral sequences have been detected and whose peptide sequence comprises at least one sequence chosen from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, said polypeptide having no more than 20 amino acids.

8. Polypeptide of claim 7, said polypeptide having no more than 15 amino acids.

9. Reagent for the detection of an MSRV-1 virus infection, characterized in that it comprises at least one polypeptide according to claim 7, said polypeptide being optionally labeled.

10. Polypeptide capable of reacting with at least one antibody in at least one biological fluid from a patient in whom MSRV-1 viral sequences have been detected and whose peptide sequence consists of a sequence chosen from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4.

11. Kit for the detection of multiple sclerosis in a patient and/or the monitoring of a patient suffering from multiple sclerosis, comprising: a reagent for the detection of multiple sclerosis in a patient and/or the monitoring of a patient suffering from multiple sclerosis, the reagent comprising at least one polypeptide capable of reacting specifically with the antibodies of patients suffering from multiple sclerosis (MS) and whose peptide sequence comprises at least one sequence chosen from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 8; SEQ ID NO: 12 to SEQ ID NO: 14, SEQ ID NO: 16 and SEQ ID NO: 19; the polypeptide having no more than 20 amino acids; and the polypeptide being optionally labeled wherein the reagent is supported on a support which is immunologically compatible with said reagent.

12. Kit for the detection of an MSRV-1 virus infection, comprising: a reagent for the detection of an MSRV-1 virus infection; the reagent comprising at least one polypeptide capable of reacting with at least one biological fluid from a patient in whom the MSRV-1 viral sequences have been detected and whose peptide sequence comprises at least one sequence chosen from SEQ ID NO: 1 to SEQ ID NO: 4; the polypeptide having no more than 20 amino acids; and the polypeptide being optionally

labeled; wherein the reagent is supported on a support which is immunologically compatible with said reagent.

13. Method of binding, in a biological sample, antibodies which are characteristic of and/or specific to multiple sclerosis, comprising: bringing the sample into contact with a reagent for the detection of multiple sclerosis in a patient and/or the monitoring of a patient suffering from multiple sclerosis, the reagent comprising at least one polypeptide capable of reacting specifically with the antibodies of patients suffering from multiple sclerosis (MS) and whose peptide sequence comprises at least one sequence chosen from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 12 to SEQ ID NO: 14, SEQ ID NO: 16 and SEQ ID NO: 19; the polypeptide having no more than 20 amino acids; and the polypeptide being optionally labeled; optionally detecting the presence of an immune complex; and optionally separating the detected immune complex.

14. Method according to claim 13, characterized in that the biological sample is chosen from serum, cerebrospinal fluid and urine.

15. Method of binding, in a biological sample, antibodies directed against the MSRV-1 virus, comprising: bringing the sample into contact with a reagent for the detection of an MSRV-1 virus infection; the reagent comprising at least one polypeptide capable of reacting with at least one biological fluid from a patient in whom the MSRV-1 viral sequences have been detected and whose peptide sequence comprises at least one sequence chosen from SEQ ID NO: 1 to SEQ ID NO: 4; the polypeptide having no more than 20 amino acids; and the polypeptide being optionally labeled; optionally detecting the presence of an immune complex; and optionally separating the detected immune complex.

16. Kit for the detection of multiple sclerosis in a patient and/or the monitoring of a patient suffering from multiple sclerosis, comprising: a reagent for the detection of multiple sclerosis in a patient and/or the monitoring of a patient suffering from multiple sclerosis; the reagent comprising at least one polypeptide capable of reacting specifically with the antibodies of patients suffering from multiple sclerosis (MS) and whose peptide sequence comprises at least one sequence chosen from SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 12 to SEQ ID NO: 14, SEQ ID NO: 16 and SEQ ID NO: 19; the polypeptide having no more than 20 amino acids; and the polypeptide being optionally labeled; wherein the reagent is supported on a support that does not react with the reagent.

17. Kit for the detection of an MSRV-1 virus infection, comprising: a reagent for the detection of an MSRV-1 virus infection; the reagent comprising at least one polypeptide capable of reacting with at least one biological fluid from a patient in whom the MSRV-1 viral sequences have been detected and whose peptide sequence comprises at least one sequence chosen from SEQ ID NO: 1 to SEQ ID NO: 4; the polypeptide having no more than 20 amino acids; and the polypeptide being optionally labeled; wherein the reagent is supported on a support that does not react with the reagent.

L3 ANSWER 3 OF 16 USPATFULL on STN
2002:19207 Cell lines and viral isolates associated with multiple sclerosis.
Perron, Herve, Grenoble, FRANCE
Mallet, Francois, Villeurbanne, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE

Bedin, Frederic, Lyons, FRANCE
Beseme, Frederic, Villefontaine, FRANCE
Bio Merieux, Marcy l'Etoile, FRANCE (non-U.S. corporation)
US 6342383 B1 20020129
APPLICATION: US 1998-133411 19980813 (9)
PRIORITY: FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-1529 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; GRANTED.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Composition comprising two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family of endogenous retroviral elements, or a variant of said virus, and a second agent, or a variant of said second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8 1993 under Accession Number V93010816, and from their variant strains.

CLM What is claimed is:

1. A continuous cell line designated LM7PC as deposited with the ECACC on Jan. 8, 1993 under Accession Number 93010817.

2. An isolated viral strain selected from the group consisting of: (a) a viral strain MS7PG deposited at the ECACC on Jan. 8, 1993 under Accession Number V93010816; (b) a viral strain obtained by culture of said viral strain MS7PG; (c) a viral strain obtainable from a cell line LM7PC, deposited at the ECACC on Jan. 8, 1993 under Accession Number 93010817; and (d) a viral strain from cells obtained by culture of said cell line LM7PC.

3. A continuous cell line obtained by culture of a viral strain of claim 2.

4. The isolated viral strain of claim 2, wherein said isolated viral strain is said viral strain MS7PG.

5. The isolated viral strain of claim 2, wherein said isolated viral strain is said viral strain obtained by culture of said viral strain MS7PG.

6. The isolated viral strain of claim 2, wherein said isolated viral strain is said viral strain obtainable from said cell line LM7PC.

7. The isolated viral strain of claim 2, wherein said isolated viral strain is said viral strain from cells obtained by culture of said cell line LM7PC.

8. An isolated viral strain selected from the group consisting of: (a) a viral strain MS7PG deposited at the ECACC on Jan. 8, 1993 under Accession Number V93010816; and (b) a viral strain obtainable from a cell line LM7PC, deposited at the ECACC on Jan. 8, 1993 under Accession Number 93010817.

2001:158057 Process and culture medium for the production of cells infected by a multiple sclerosis-associated virus.

Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)

US 6291225 B1 20010918
APPLICATION: US 1995-485145 19950607 (8)
PRIORITY: FR 1992-4322 19920403
FR 1992-13443 19921103
DOCUMENT TYPE: Utility; GRANTED.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Process for in vitro production of a culture or cell line infected by a viral strain associated with multiple sclerosis (MS), according to which a body sample is taken from an individual suffering from MS, the sample is cultivated in a culture medium which promotes the growth of infected cells to obtain a culture of primary infected cells, and a sample of the culture of primary cells or of a subculture of the latter is cultivated in series, that is to say by successive passages, in the culture medium to obtain the culture or cell line infected by a virus associated with MS. The process includes a procedure in which the culture medium also contains a beta anti-interferon antibody or an antibody which is directed against an antigenically close molecule, the antibody playing an inhibiting role in viral expression and allowing long-lasting expression and propagation of the viral strain in the culture or cell line.

CLM What is claimed is:

1. A viral biological material selected from the group consisting of: (a) a viral strain POL-2 deposited at the ECACC on Jul. 22, 1992 under number V92072202; (b) a viral strain obtained by culture of said viral strain POL-2; (c) a viral strain obtainable from a cell line PLI-2, deposited at the ECACC on Jul. 22, 1992 under number 92072201; and (d) a viral strain from cells obtained by culture of said cell fine PLI-2.

2. The viral biological material of claim 1, wherein said viral biological material is being said viral strain POL-2 deposited at the ECACC on Jul. 22, 1992 under number V92072202.

3. The viral biological material of claim 1, wherein said viral biological material is said viral strain obtained by culture of said viral strain POL-2.

4. The viral biological material of claim 1, wherein said viral biological material is being said viral strain composition obtainable from said cell line PLI-2, deposited at the ECACC on Jul. 22, 1992 under number 92072201.

5. The viral biological material of claim 1, wherein said viral biological material is said viral strain from cells obtained by culture of said cell line PLI-2.

6. The viral biological material of claim 1, wherein said cell line PLI-2 is transfected by at least one immediate early gene of HSV-1 virus.

7. The viral biological material of claim 6, wherein said immediate early gene is selected from the group consisting of a gene which codes for a protein ICPO of HSV-1 virus and a gene which codes for a protein ICP4 of HSV-1 virus.

8. A viral biological material selected from the group consisting of:

(a) a viral strain POL-2 deposited at the ECACC on Jul. 22, 1992 under number V92072202 and (b) a viral strain obtainable from a cell line PLI-2, deposited at the ECACC on Jul. 22, 1992 under number 92072201.

L3 ANSWER 5 OF 16 USPATFULL on STN
2001:125726 Method for detecting and/or quantifying a gliotoxic factor.
Malcus-Vocanson, Carine, Brignais, France
Perron, Herve, Lyons, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6270953 B1 20010807
WO 9811439 19980319
APPLICATION: US 1999-202118 19990329 (9)
WO 1997-FR1620 19970912 19990329 PCT 371 date 19990329 PCT 102(e) date
PRIORITY: FR 1996-11347 19960912
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention proposes a method for detecting and/or quantifying, in a biological sample, a cytotoxic factor, in particular a gliotoxic factor, with respect to adherent target cells, in particular macroglial cells, the toxicity of which causes the death by apoptosis of said cells. The method comprises providing an initial fraction of the sample, optionally enriched with the toxic factor by previous treatment, incubating the initial toxic factor with a reference culture medium comprising adherent target cells, and detecting and/or quantifying in the adherent target cells killed by apoptosis, by flow cytometry, at least one direct or indirect characteristic associated with the apoptotic adherent cells of the whole or part of the incubated medium, which, if it is present and/or is quantified, qualifies the sample as positive, i.e. as containing said toxic factor. The initial biological sample is preferably a urine specimen.

CLM What is claimed is:

1. A process for detecting, in a urine sample, a factor that is cytotoxic for target adherent macroglial cells and whose cytotoxicity induces death of said cells by apoptosis, said process comprising: incubating said sample with a reference culture medium comprising said target macroalial adherent cells; and detecting and/or quantifying the target adherent macroglial cells that have died by apoptosis using flow cytometry, thereby indicating the presence of a cytotoxic factor in the biological sample.

2. A process according to claim 1, wherein the target adherent macroglial cells are astrocytic cells.

3. A process according to claim 1, wherein said process of detecting and/or quantifying the target adherent macroglial cells that have died by apoptosis comprises: detaching the adherent macroglial cells, treating the cells that have thus been detached with an agent for cell fixation and permeabilization of the cytoplasmic membrane of said cells, extracting intracellular DNA fragments resulting from apoptosis, labeling the remaining cellular DNA with an appropriate label, adjusting the flow cytometer to exclude the cells which have died by necrosis, and detecting, by flow cytometry, the ploidy of the macroglial cells, thereby detecting the cells that have died by apoptosis.

4. A process according to claim 3, wherein the agent for cell fixation and permeabilization of the cytoplasmic membrane of the cells is ethanol.

5. A process according to claim 3, wherein the label for the DNA is propidium iodide (PI).

6. A process according to claim 3 in which the cells which have died by necrosis are determined by: inducing necrosis in a second sample of living macroglial cells, detaching the cells, labeling the DNA debris resulting from necrosis, said debris being associated with fragments of the cytoplasmic membrane of the necrotic macroglial cells, and detecting and/or quantitating the cells that have died by necrosis.

7. A process according to claim 1, wherein said process of detecting and/or quantifying the target macroglial cells that have died by apoptosis using flow cytometry comprises: dividing the cells in the reference culture medium containing the incubated sample into two equal parts and detaching the cells, and in one part, the cells are treated with an agent for cell fixation and for permeabilization of the cytoplasmic membrane, the DNA fragments are extracted the remaining intracellular DNA is labeled and detected by flow cytometry, thereby distinguishing the living cells from the cells that have died by necrosis or apoptosis, in the second part, the cells are treated with an agent for cell fixation and the remaining intracellular DNA is labeled and detected by flow cytometry, thereby distinguishing the living cells and the cells that have died by apoptosis from the cells that have died by necrosis, and deducing, from the detection and/or quantification of part one and part two, the quantity of apoptotic macroglial cells.

8. A process according to claim 1, wherein the reference culture medium comprises an immortalized cell line of cells.

9. A process according to claim 8, wherein said immortalized cell line is an astrocyte cell line.

10. A process according to claim 1, wherein, prior to detecting and/or quantifying the target macroglial cells that have died by apoptosis, the cell viability is detected, said process comprising: comparing the rate of macroglial cell proliferation in the reference culture medium with a value obtained from untreated macroglial cells in culture medium.

11. A process according to claim 10, wherein during the step of detecting cell viability, the rate of proliferation of the macroglial cells is obtained by staining the mitochondria of the macroglial cells in the culture medium and then measuring the optical density of the cells in the culture medium.

12. A process according to claim 11, wherein the mitochondria is stained with methyltetrazolium bromide.

13. A process according to claim 1, wherein, during the step of detecting and/or quantifying the target macroglial cells that have died by apoptosis, the presence and/or quantity of a protein is determained to discriminate between subpopulations of cells.

14. A process according to claim 13, wherein said protein is a glial fibrillary acidic protein (GFAP).

15. A process according to claim 14, wherein the presence and/or quantity of said GFAP protein is determined using an anti-GFAP antibody.

16. A process according to claim 1, wherein, prior to incubating the sample with a reference culture medium, said sample has been enriched in

said cytotoxic factor.

17. A process according to claim 16, wherein the cytotoxic factor in the urine sample enriched or purified using at least one treatment selected from the group consisting of precipitation of the protein fraction, exclusion and/or ion exchange chromatography, one-dimensional or two-dimensional electrophoresis, two bringing the sample into contact with protein A or a lectin.

18. A process for detecting, in a biological sample, a factor that is gliotoxic for target macroglial cells, wherein the biological sample is a urine sample, said process comprising: incubating said sample with a reference culture medium comprising said target macroglial cells; and detecting and/or quantifying the target macroglial cells that have died by apoptosis, thereby detecting the presence of a gliotoxic factor in the biological sample.

19. A process according to claim 18, wherein, prior to detecting and/or quantifying the target macroglial cells that have died by apoptosis, the cell viability is detected, said process comprising: comparing the rate of macroglial cell proliferation in the reference culture medium with a value obtained from untreated macroglial cells in culture medium.

20. A process according to claim 19, wherein during the step of detecting cell viability, the rate of proliferation of the macroglial cells is obtained by staining the mitochondria the macroglial cells in the culture medium and then measuring the optical density of the cells in the culture medium.

21. A process according to claim 18, wherein said gliotoxic factor is associated with multiple sclerosis.

22. A process according to claim 18, wherein, prior to incubating the sample with a reference culture medium, said sample has been enriched in said gliotoxic factor.

23. A process according to claim 22, wherein the gliotoxic factor in the urine sample is enriched or purified using at least one treatment selected from the group consisting of precipitation of the protein fraction, exclusion and/or ion exchange chromatography, one-dimensional or two-dimensional electrophoresis, and bringing the sample into contact with protein A or a lectin.

24. A process according to claim 23, wherein the protein fraction is precipitated with ammonium sulfate.

25. A process according to claim 23, wherein said protein A or lectin is concanavalin A.

L3 ANSWER 6 OF 16 USPATFULL on STN
2001:18272 Viral isolates associated with multiple sclerosis.
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyon, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6184025 B1 20010206
APPLICATION: US 1998-200990 19981130 (9)

PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition comprising two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family of endogenous retroviral elements, or a variant of said virus, and a second agent, or a variant of said second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, and from their variant strains.
CLM What is claimed is:

1. An isolated viral strain designated POL-2 as deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202, or designated MS7PG as deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, or any naturally occurring variant strains of said viral strains POL-2 and MS7PG.

2. A virus, in the purified or isolated state, possessing reverse transcriptase activity, associated with a family of endogenous retroviral elements and associated with multiple sclerosis, originating from a viral strain possessing reverse transcriptase activity, selected from the group consisting of a viral strain designated POL-2 as deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202, a viral strain designated MS7PG as deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816 and any naturally occurring variant strains of said viral strains POL-2 and MS7PG.

3. An isolated virus comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, their complementary sequences and their equivalent sequences, said equivalent sequences displaying, for any succession of 100 contiguous monomers, at least 50% identity with a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6; SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

4. An isolated retrovirus associated with multiple sclerosis, characterized in that the pol gene of its genome comprises an equivalent nucleotide sequence, said equivalent sequence displaying at least 50% identity with a nucleotide sequence belonging to the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

5. An isolated retrovirus associated with multiple sclerosis, characterized in that the pol gene of its genome codes for a peptide sequence displaying at least 50% identity with a peptide sequence encoded by the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

6. An isolated retrovirus associated with multiple sclerosis, characterized in that the pol gene of its genome codes for a peptide sequence displaying, for any contiguous succession of at least 30 amino acids, at least 50% identity with a peptide sequence encoded by a

nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

7. The isolated virus according to claim 3, wherein said equivalent sequences display, for any succession of 100 contiguous monomers, at least 70% identity with a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

8. The retrovirus according to claim 4, wherein said equivalent nucleotide sequence displays at least 65% identity with nucleotide sequences belonging to the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

9. The retrovirus according to claim 5, wherein said pol gene coding for a peptide sequence displays at least 70% identity with a peptide sequence encoded by the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

10. The retrovirus according to claim 5, characterized in that the pol gene of its genome codes for a peptide sequence displaying, for any contiguous succession of at least 30 amino acids, at least 50% identity with a peptide sequence encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

11. The retrovirus according to claim 10, wherein said pol gene codes for a peptide sequence displaying, for any contiguous succession of at least 30 amino acids, at least 70% identity with a peptide sequence encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

12. The retrovirus according to claim 6, wherein said pol gene codes for a peptide sequence displaying, for any contiguous succession of at least 30 amino acids, at least 70% identity with a peptide sequence encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

13. The retrovirus according to claim 6, characterized in that the pol gene of its genome codes for a peptide sequence displaying at least 50% identity with a peptide sequence encoded by the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

14. The retrovirus according to claim 13, wherein said pol gene codes for a peptide sequence displaying at least 70% identity with a peptide sequence encoded by the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

L3 ANSWER 7 OF 16 USPATFULL on STN
2000:70666 Process and culture medium for the production of cells infected by a multiple sclerosis-associated virus.

Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6071736 20000606
APPLICATION: US 1996-754010 19961120 (8)
PRIORITY: FR 1992-13443 19921103
FR 1993-9204322 19930403
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB In a process for the in vitro production of a culture or cell line infected by a viral strain associated with multiple sclerosis (MS), a body sample is taken from an individual suffering from MS. The sample is cultivated in a culture medium that promotes the growth of infected cells to obtain a culture of primary infected cells. A sample of the culture of primary cells or a subculture of the latter is cultivated in series, by successive passages in the culture medium to obtain the culture or cell line infected by a virus associated with MS. The culture medium also contains a beta-interferon antibody or an antibody that is directed against an antigenically close molecule, the antibody playing an inhibiting role in viral expression and allowing long-lasting expression and propagation of the viral strain in the culture or cell line.

CLM What is claimed is:

1. A process for in vitro production of a culture or cell line infected by a viral strain, said viral strain having at least one of its replication and expression inhibited by a molecule which plays an inhibiting role in viral expression, said process comprising: obtaining a body sample from an individual infected with said viral strain, cultivating said body sample in a culture medium which promotes growth of infected cells to obtain a culture or cell line of primary infected cells, and cultivating by successive passages in said culture medium a sample of the culture or cell line of primary infected cells or a subculture of said culture or cell line to obtain the culture or cell line infected by said viral strain, wherein the culture medium also contains an antibody directed against said molecule which plays an inhibiting role in viral expression, and said culture medium allows persistent expression and propagation of the viral strain in the culture or cell line.

2. A culture medium for carrying out a process as claimed in claim 1, comprising at least one amino acid, at least one vitamin factor, at least one inorganic salt, glucose, and said antibody directed against said molecule which plays an inhibiting role in viral expression.

3. The culture medium according to claim 2, further comprising said viral strain.

4. The process according to claim 1, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon or a molecule antigenically close to beta-interferon.

5. The process according to claim 4, wherein said viral strain is associated with multiple sclerosis.

6. The process according to claim 1, wherein said viral strain is associated with multiple sclerosis.

7. The culture medium according to claim 2, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon or a molecule antigenically close to beta-interferon.

8. The culture medium according to claim 3, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon or a molecule antigenically close to beta-interferon.

9. The culture medium according to claim 3, wherein said viral strain is associated with multiple sclerosis.

10. The culture medium according to claim 8, wherein said viral strain is associated with multiple sclerosis.

11. The process according to claim 4, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon.

12. The culture medium according to claim 7, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon.

13. The culture medium according to claim 8, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon.

L3 ANSWER 8 OF 16 USPATFULL on STN
1999:121120 MSRV1 virus and MSRV2 pathogen and/or infective agent associated with multiple sclerosis, and biopolymer constituents thereof.
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy I'Etoile, France (non-U.S. corporation)
US 5962217 19991005
APPLICATION: US 1995-470006 19950606 (8)
PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition including two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family of endogenous retroviral elements, or a variant of the virus, and a second agent, or a variant of the second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, and from their variant strains.
CLM What is claimed is:
1. An isolated or synthetic nucleotide fragment comprising a first nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, a fragment of SEQ ID NO:12 comprising at least 100 contiguous monomers of SEQ ID NO:12, and a complementary sequence complementary to one of said SEQ ID NO:10 through SEQ ID NO:15, SEQ ID NO:27 through SEQ ID NO:30, SEQ ID NO:34 through SEQ ID NO:37 or said fragment of SEQ ID NO:12.

2. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:10, or its complementary sequence.

3. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:11, or its complementary sequence.

4. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is selected from the group consisting of SEQ ID NO:12, a fragment of SEQ ID NO:12 comprising at least 100 contiguous monomers of SEQ ID NO:12 and a complementary sequence complementary to one of said SEQ ID NO:12 or said fragment of SEQ ID NO:12.

5. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:13, or its complementary sequence.

6. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:14, or its complementary sequence.

7. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:15, or its complementary sequence.

8. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:27, or its complementary sequence.

9. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:28, or its complementary sequence.

10. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:29, or its complementary sequence.

11. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:30, or its complementary sequence.

12. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:34, or its complementary sequence.

13. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:35, or its complementary sequence.

14. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:36, or its complementary sequence.

15. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:37, or its complementary sequence.

16. A specific primer for amplification by polymerization of a nucleic acid of a pathogenic or infectious agent associated with multiple sclerosis, said primer comprising at least six contiguous monomers of the nucleotide sequence of the nucleotide fragment according to claim 1.

17. The primer according to claim 16, wherein said nucleotide sequence is selected from the group consisting of SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, and a complementary sequence complementary to one of said SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, or SEQ ID NO:37.

18. A probe for specifically hybridizing with a nucleic acid of a

pathogenic or infectious agent associated with multiple sclerosis, said probe comprising at least six contiguous monomers of the nucleotide sequence of the nucleotide fragment according to claim 1.

19. The probe according to claim 18, wherein said nucleotide sequence is selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, and a complementary sequence complementary to one of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, or SEQ ID NO:37.

20. A replication vector comprising the nucleotide fragment according to claim 1 and a promoter sequence.

21. A diagnostic, composition comprising a nucleotide fragment according to claim 1.

22. An isolated pathogenic or infectious agent associated with multiple sclerosis, said agent having a genome comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, a fragment of SEQ ID NO:12 comprising at least 100 contiguous monomers of SEQ ID NO:12, and a complementary sequence complementary to one of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 or said fragment of SEQ ID NO:12.

23. The agent according to claim 22, said agent having a genome comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and a complementary sequence complementary to one of said SEQ ID NO:10, SEQ ID NO:1I or SEQ ID NO:12.

L3 ANSWER 9 OF 16 USPATFULL on STN

1999:81747 Process for the production of a viable cell culture infected by a multiple sclerosis-associated virus.

Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, L'Etoile, France (non-U.S. corporation)Universite Joseph Fourier (Grenoble 1), Grenoble Cedex, France (non-U.S. corporation)

US 5925555 19990720
APPLICATION: US 1996-651573 19960522 (8)
PRIORITY: FR 1992-4322 19920403
FR 1992-13447 19921103
DOCUMENT TYPE: Utility; Granted.

AB The present invention relates to a process for in vitro culture of cells infected by a virus associated with multiple sclerosis and to the infected cell lines thus produced. According to the invention, the process includes: a) cultivation of human cells infected by a viral strain to obtain at least one culture of primary cells infected by the viral strain, b) cultivation of non-infected human cells permissive to the viral strain to obtain at least one permissive culture, c) cocultivation of at least one sample of a culture of infected primary cells and one sample of the permissive culture to obtain a first infected derived culture, d) cultivation in series of the first infected derived culture. The invention is used in particular in the pharmaceutical diagnostics industry sector.

CLM What is claimed is:

1. A process for producing a viable infected culture or cell line comprising cells infected by at least one human viral strain associated

with multiple sclerosis (MS) having reverse transcriptase activity, said process comprising: (a) cultivating cells infected by said viral strain to obtain at least one culture or cell line of primary cells infected by said viral strain, (b) cultivating non-infected leptomeningeal or plexus choroideus cells that are permissive to said viral strain to obtain at least one non-infected permissive culture, (c) cocultivating at least one sample of said culture or cell line of primary infected cells and at least one sample of said at least one non-infected permissive culture to obtain a first derived culture of leptomeningeal or plexus choroideus cells infected by said viral strain, and (d) cultivating the first infected derived culture in series, by cocultivating a new sample of the at least one non-infected permissive culture and a sample of the first infected derived culture, or of a subculture of the first infected derived culture, to obtain a new subculture of the first infected derived culture, constituting a viable viral culture or cell line.

2. The process as claimed in claim 1, wherein the culture or cell-line of infected primary cells is obtained from cells infected by said viral strain, said cells being selected from the group consisting leptomeningeal cells, plexus choroideus cells, myeloid blood cells and lymphocytes.

3. The process as claimed in claim 1, wherein the permissive culture is obtained from human plexus choroideus cells.

4. The process as claimed in claim 1, wherein several of said primary cultures infected by differing viral strains are obtained in step (a), and wherein step (c) is carried out by cocultivating a sample of the permissive culture and several differing samples of said infected primary cultures.

5. The process as claimed in claim 1, further comprising providing a culture medium for cultivating said permissive cells, wherein said culture medium comprises: between 400 and 2250 mg/l of amino acids; between 3.5 and 130 mg/l of vitamins; between 9100 and 13,000 mg/l of inorganic salts; and between 1000 and 6000 mg/l of glucose.

6. A viable cell culture infected by a human viral strain associated with multiple sclerosis, which comprises viable cells sampled from or belonging to a viable infected culture or cell line obtained by a process as claimed in claim 1, or viable derived cells obtained by modifying the genome of said cells, without altering their phenotype.

7. The process as claimed in claim 1, wherein the culture of infected primary cells is obtained from cells infected by said viral strain and selected from the group consisting of macrophages and monocytes.

8. The process as claimed in claim 5, wherein said culture medium further comprises at least one growth factor selected from the group consisting of endothelial cell growth factor and basic fibroblast growth factor.

9. The process as claimed in claim 1, wherein said at least one culture or cell line is an LM7-type culture or cell line.

10. A process for producing a viable infected culture or cell line comprising cells infected by at least one human viral strain associated with multiple sclerosis (MS) having reverse transcriptase activity, said process comprising: (a) cultivating cells infected by said viral strain and selected from the group consisting of leptomeningeal cells, plexus

choroideus cells, myeloid blood cells and lymphocytes, to obtain at least one culture or cell line of primary cells infected by said viral strain, (b) cultivating plexus choroideus cells that are permissive to said viral strain to obtain at least one non-infected permissive culture, (c) cocultivating at least one sample of said culture or cell line of primary infected cells and at least one sample of said at least one non-infected permissive culture to obtain a first derived culture of plexus choroideus cells infected by said viral strain, and (d) cultivating the first infected derived culture in series, by cocultivating a new sample of the at least one non-infected permissive culture and a sample of the first infected derived culture or of a subculture of the first infected derived culture to obtain a new subculture of the first infected derived culture, constituting a viable viral culture or cell line.

11. The process as claimed in claim 10, wherein said human cells are LM7-type cells.

12. A process for producing a viable infected culture or cell line comprising cells infected by multiple sclerosis (MS), said process comprising: (a) cultivating cells infected with MS to obtain at least one culture or cell line of primary infected cells, (b) cultivating non-infected leptomeningeal or plexus choroideus cells that are permissive to MS to obtain at least one non-infected permissive culture, (c) cocultivating at least one sample of said culture or cell line of primary infected cells and at least one sample of said at least one non-infected permissive culture to obtain a first infected derived culture, and (d) cultivating the first infected derived culture in series, by cocultivating a new sample of the at least one non-infected permissive culture and a sample of the first infected derived culture or of a subculture of the first infected derived culture to obtain a new subculture of the first infected derived culture, constituting a viable culture or cell line.

13. The process as claimed in claim 1, wherein said infected and non-infected cells are nervous system cells.

14. The process as claimed in claim 1, wherein the permissive culture is obtained from plexus choroideus cells.

15. The process as claimed in claim 1, wherein the infected and non-infected cells are human cells.

16. The process as claimed in claim 10, wherein the infected and non-infected cells are human cells.

L3 ANSWER 10 OF 16 USPATFULL on STN
1999:27417 Cytotoxic factor as is associated with multiple sclerosis, its detection and its quantification.
Perron, Herve, Grenoble, France
Dobransky, Tomas, Marly-le-Roy, France
Rieger, Fran.cedilla.ois, Paris, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5876954 19990302
APPLICATION: US 1995-389164 19950215 (8)
PRIORITY: FR 1994-1946 19940215
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Gliotoxic factor in the isolated or purified state, characterized in that it possesses toxic activity with respect to human or animal astrocytic cells, having the effect of a cytomorphological disorganization of their network of intermediate filaments and/or a degradation of the proteins of said intermediate filaments and/or cell death, in particular by apoptosis.

CLM What is claimed is:

1. An isolated or purified protein gliotoxic factor having toxic activity with respect to astrocytic cells, wherein said toxic activity is expressed as cell death by apoptosis.

2. The gliotoxic factor according to claim 1, wherein said toxic activity is associated with at least one globular glycoprotein.

3. The gliotoxic factor according to claim 1, comprising a light fraction centered around an apparent molecular weight of approximately 17 kD, and a less abundant heavy fraction centered around an apparent molecular weight of approximately 21 kD, at least said light fraction being resistant, under nondenaturing conditions, to a hydrolytic action of at least one enzyme selected from the group consisting of pronase, trypsin and proteinase K, each of the two said fractions displaying affinity for at least one lectin.

4. A method for obtaining an isolated or purified gliotoxic factor having toxic activity with respect to astrocytic cells, wherein said toxic activity is expressed as cell death, said method comprising: obtaining a biological sample, treating said sample on an ion exchange resin, and treating said ion-exchanged sample on a column for separation by exclusion, to obtain said gliotoxic factor.

5. A gliotoxic factor according to claim 3, wherein said at least one lectin is concanavalin A.

6. The method according to claim 4, wherein said sample is obtained from a patient suffering from an autoimmune disorder.

7. An isolated or purified gliotoxic factor having an apparent molecular weight of approximately 17 kD, that is resistant, under nondenaturing conditions, to a hydrolytic action of at least one enzyme selected from the group consisting of pronase, trypsin and proteinase K, and that displays affinity for at least one lectin, said gliotoxic factor having toxic activity with respect to astrocytic cells, wherein said toxic activity is expressed as cell death.

8. The gliotoxic factor according to claim 1, having an apparent molecular weight of approximately 21 kD and displaying affinity for at least one lectin.

9. An isolated or synthetic antibody specific to the gliotoxic factor according to claim 1.

10. The method according to claim 4, wherein said sample is obtained from a patient suffering from a neurological disorder.

11. The method according to claim 4, wherein said sample is obtained from a patient suffering from multiple sclerosis.

12. The method according to claim 11, wherein said sample is obtained from serum or spinal fluid of said patient.

13. The gliotoxic factor according to claim 1, wherein said toxic activity is furthermore expressed as at least one of cytomorphological disorganization of a network of intermediate filaments of said astrocytic cells and protein degradation of said network of intermediate filaments.

14. The method according to claim 4, wherein said gliotoxic factor comprises a light fraction centered around an apparent molecular weight of approximately 17 kD, and a less abundant heavy fraction centered around an apparent molecular weight of approximately 21 kD, at least said light fraction being resistant, under nondenaturing conditions, to a hydrolytic action of at least one enzyme selected from the group consisting of pronase, trypsin and proteinase K, each of the two said fractions displaying affinity for at least one lectin.

15. The method according to claim 4, wherein said cell death is by apoptosis.

16. The gliotoxic factor according to claim 7, wherein said cell death is by apoptosis.

17. A pharmaceutical or diagnostic composition comprising a pharmaceutical- or diagnostic-effective amount of a protein gliotoxic factor having toxic activity with respect to astrocytic cells, wherein the toxic activity is expressed as cell death by apoptosis.

18. A pharmaceutical or diagnostic composition comprising a ligand specific to a protein gliotoxic factor having toxic activity with respect to astrocytic cells, wherein the toxic activity is expressed as cell death by apoptosis.

19. The method according to claim 14, wherein said at least one lectin is concanavalin A.

20. The pharmaceutical or diagnostic composition according to claim 18, wherein said ligand is an antibody.

L3 ANSWER 11 OF 16 USPATFULL on STN
1999:21977 Retrovirus agents MSRV1 and MSRV2 associated with multiple sclerosis

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Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5871996 19990216
APPLICATION: US 1995-384137 19950206 (8)
PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition including two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family

of endogenous retroviral elements, or a variant of the virus, and a second agent, or a variant of the second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, and from their variant strains.

CLM What is claimed is:

1. A composition comprising: a first agent comprising an isolated virus, wherein said virus possesses reverse transcriptase activity, and a second agent, wherein said second agent is distinct from said virus of said first agent and comprises nucleotides, wherein said first and second agents are associated with multiple sclerosis and are both purifiable from a viral isolate selected from the group consisting of POL-2 (ECAC V92072202) and MS7PG (ECAC V93010816).

2. A composition comprising: a first agent comprising an isolated virus, wherein said virus possesses reverse transcriptase activity, and a second agent, wherein said second agent is distinct from said virus of said first agent and comprises nucleotides, wherein said first and second agents are associated with multiple sclerosis and are both purifiable from a cell line selected from the group consisting of PLI-2 (ECAC 92072201) and LM7PC (ECAC 93010817).

3. A composition comprising: a first agent comprising an isolated virus which possesses reverse transcriptase activity, wherein said virus comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO;3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, and sequences complementary to each of said SEQ ID NO:1 through SEQ ID NO:9; and a second agent distinct from said first agent, wherein said second agent comprises at least one antigen and a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and sequences complementary to each of said SEQ ID NO:10 through, SEQ ID NO:12.

4. The composition according to claim 1, wherein said first agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, and sequences complementary to each of said SEQ ID NO:1 through SEQ ID NO:9.

5. The composition according to claim 1, wherein said second agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and sequences complementary to each of said SEQ ID NO:10, SEQ ID NO:11 and SEQ NO:12.

6. The composition according to claim 4, wherein said second agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and sequences complementary to each of said SEQ ID NO:10, SEQ ID NO:11 and SEQ ID NO:12.

7. The composition according to claim 2, wherein said first agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, and sequences complementary to each of said SEQ ID NO:1 through SEQ ID NO:9.

8. The composition according to claim 2, wherein said second agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and sequences complementary to

each of said SEQ ID NO:10, SEQ ID NO:11 and SEQ NO:12.

9. The composition according to claim 7, wherein said second agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and sequences complementary to each of said SEQ ID NO:10, SEQ ID NO:11 and SEQ ID NO:12.

L3 ANSWER 12 OF 16 USPATFULL on STN
1999:21732 Multiple sclerosis related virus.
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 5871745 19990216
APPLICATION: US 1995-471969 19950606 (8)
PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition including two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family of endogenous retroviral elements, or a variant of the virus, and a second agent, or a variant of the second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, and from their variant strains.
CLM What is claimed is:
1. An isolated virus comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, and complementary sequences complementary thereto.

2. The isolated virus according to claim 1, wherein the nucleotide sequence is SEQ ID NO: 1 or a sequence complementary thereto.

3. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 2 or a sequence complementary thereto.

4. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 3 or a sequence complementary thereto.

5. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 4 or a sequence complementary thereto.

6. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 5 or a sequence complementary thereto.

7. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 6 or a sequence complementary thereto.

8. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 7 or a sequence complementary thereto.

9. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 8 or a sequence complementary thereto.

10. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 9 or a sequence complementary thereto.

L3 ANSWER 13 OF 16 USPATFULL on STN

1998:104553 Detection of MSRV1 virus and MSRV2 pathogen and/or infective agent associated with multiple sclerosis, by nucleic acid hybridization.

Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5800980 19980901
APPLICATION: US 1995-471724 19950606 (8)
PRIORITY: FR 1999-9401529 18990204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Composition including two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family of endogenous retroviral elements, or a variant of the virus, and a second agent, or a variant of the second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, and from their variant strains.

CLM What is claimed is:

1. A method for distinguishing, in a biological sample, a viral material, said method comprising contacting at least one nucleic acid from said biological sample, or at least one complementary nucleic acid complementary to said at least one nucleic acid, with at least one probe which hybridizes with a nucleic acid of said viral material, said probe comprising a first nucleotide sequence selected from the group consisting of (i) SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, (ii) a first complementary sequence fully complementary to one of said SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:20 through SEQ ID NO:26 or SEQ ID NO:31 through SEQ ID NO:33, and (iii) a first homologous sequence sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20 through SEQ ID NO:26, SEQ ID NO:31 through SEQ ID NO:33, or said first complementary sequence, to hybridize to a nucleic acid sequence of MSRV-1 and not hybridize to a nucleic acid sequence of HSERV9; and distinguishing in said biological sample any said viral material having a sequence hybridized to said at

least one probe.

2. The method according to claim 1, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one specific primer comprising a second nucleotide sequence selected from the group consisting of (i) SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, (ii) a second complementary sequence fully complementary to one of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26 or SEQ ID NO:31 through SEQ ID NO:33, and (iii) a second homologous sequence sufficiently homologous with at least one second segment of at least 6 contiguous monomers of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26, SEQ ID NO:31 through SEQ ID NO:33, or said second complementary sequence, to hybridize to a nucleic acid sequence of MSRV-1 and not hybridize to a nucleic acid sequence of HSERV9.

3. A method for distinguishing, in a biological sample, at least one pathogenic or infectious agent, said method comprising contacting at least one nucleic acid from said biological sample, or at least one complementary nucleic acid complementary to said at least one nucleic acid, with at least one probe which hybridizes with a nucleic acid or a complement of a nucleic acid of said pathogenic or infectious agent, said probe comprising a first nucleotide sequence selected from the group consisting of (i) SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, (ii) a first complementary sequence fully complementary to one of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, or SEQ ID NO:37, and (iii) a first homologous sequence sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, or said first complementary sequence, to hybridize to a nucleic acid sequence of MSRV-2 and not to other naturally occurring nucleic acid sequences; and distinguishing in said biological sample any said at least one pathogenic or infectious agent having a sequence hybridized to said at least one probe.

4. The method according to claim 3, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one specific primer comprising a second nucleotide sequence selected from the group consisting of (i) SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, (ii) a second complementary sequence fully complementary to one of said SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, or SEQ ID NO:37, and (iii) a second homologous sequence sufficiently homologous with at least one second segment of at least 6 contiguous monomers of said SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, or said second complementary sequence, to hybridize to a nucleic acid sequence of MSRV-2 and not to

other naturally occurring nucleic acid sequences.

5. The method according to claim 1, wherein said at least one probe is specific for said nucleic acid or complementary nucleic acid of said viral material.

6. The method according to claim 1, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one primer.

7. The method according to claim 1, wherein a plurality of said probes are employed.

8. The method according to claim 3, wherein said at least one probe is specific for said nucleic acid or complementary nucleic acid of said pathogenic or infectious agent.

9. The method according to claim 3, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one primer.

10. The method according to claim 3, wherein a plurality of said probes are employed.

11. A method for distinguishing, in a biological sample, a viral material associated with multiple sclerosis, said method comprising contacting at least one nucleic acid from said biological sample, or at least one complementary nucleic acid complementary to said at least one nucleic acid, with at least one probe which hybridizes with a nucleic acid of said viral material, said probe comprising a first nucleotide sequence selected from the group consisting of (i) SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, (ii) a first complementary sequence fully complementary to one of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26 or SEQ ID NO:31 through SEQ ID NO:33, and (iii) a first homologous sequence sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26, SEQ ID NO:31 through SEQ ID NO:33, or said first complementary sequence, to hybridize to a nucleic acid sequence of MSRV-1 and not hybridize to a nucleic acid sequence of HSERV9; and distinguishing in said biological sample any said viral material having a sequence hybridized to said at least one probe.

12. The method according to claim 11, wherein said at least one probe is specific for said nucleic acid or complementary nucleic acid of said viral material.

13. The method according to claim 11, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one primer.

14. The method according to claim 11, wherein a plurality of said probes are employed.

15. A method for distinguishing, in a biological sample, at least one pathogenic or infectious agent associated with multiple sclerosis, said method comprising contacting at least one nucleic acid from said biological sample, or at least one complementary nucleic acid complementary to said at least one nucleic acid, with at least one probe which hybridizes with a nucleic acid or a complement of a nucleic acid of said pathogenic or infectious agent, said probe comprising a first nucleotide sequence selected from the group consisting of (i) SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, (ii) a first complementary sequence fully complementary to one of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, or SEQ ID NO:37, and (iii) a first homologous sequence sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, or said first complementary sequence, to hybridize to a nucleic acid sequence of MSRV-2 and not to other naturally occurring nucleic acid sequences; and distinguishing in said biological sample any said at least one pathogenic or infectious agent having a sequence hybridized to said at least one probe.

16. The method according to claim 15, wherein said at least one probe is specific for said nucleic acid or complementary nucleic acid of said pathogenic or infectious agent.

17. The method according to claim 15, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one primer.

18. The method according to claim 15, wherein a plurality of said probes are employed.

19. A method for distinguishing, in a biological sample, a viral material, said method comprising contacting at least one nucleic acid from said biological sample, or at least one complementary nucleic acid complementary to said at least one nucleic acid, with at least one probe of not more than 100 contiguous monomers which hybridizes with a nucleic acid of said viral material, said probe comprising a first nucleotide sequence selected from the group consisting of (i) SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, (ii) a first complementary sequence fully complementary to one of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26 or SEQ ID NO:31 through SEQ ID NO:33, and (iii) a first homologous sequence sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26, SEQ ID NO:31 through SEQ ID NO:33, or said first complementary sequence to hybridize to a nucleic acid sequence of MSRV-1 and not hybridize to a nucleic acid sequence of HSERV9; and distinguishing in said biological sample any said viral material having a sequence hybridized to said at least one probe.

20. The method according to claim 19, wherein said at least one probe is

specific for said nucleic acid or complementary nucleic acid of said viral material.

21. The method according to claim 19, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one primer.

22. The method according to claim 19, wherein a plurality of said probes are employed.

23. The method according to claim 1, wherein said first homologous sequence is sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:20 through SEQ ID NO:26, SEQ ID NO:31 through SEQ ID NO:33, or said first complementary sequence, to hybridize to a nucleic acid sequence of MSRV-1 and not hybridize to a nucleic acid sequence of HSERV9.

L3 ANSWER 14 OF 16 USPATFULL on STN
1998:27921 Cytotoxic factor as is associated with multiple sclerosis, its detection and its quantification.
Perron, Herve, Grenoble, France
Dobransky, Tomas, Marly-Le-Roy, France
Rieger, Fran.cedilla.ois, Paris, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy L'etoile, France (non-U.S. corporation)
US 5728540 19980317
APPLICATION: US 1995-468670 19950606 (8)
PRIORITY: FR 1994-1946 19940215
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Gliotoxic factor in the isolated or purified state, characterized in that it possesses toxic activity with respect to human or animal astrocytic cells, having the effect of a cytomorphological disorganization of their network of intermediate filaments and/or a degradation of the proteins of said intermediate filaments and/or cell death, in particular by apoptosis.
CLM What is claimed is:
1. A method for analyzing an activity of a pathology associated with a gliotoxic factor having toxic activity with respect to macroglial cells, said method comprising: obtaining a biological sample; incubating said sample with said macroglial cells; and assaying said gliotoxic factor in said biological sample by detecting apoptosis in said macroglial cells.

2. The method according to claim 1, wherein the pathology is multiple sclerosis.

3. A method for pretreating a biological sample comprising a gliotoxic factor having toxic activity with respect to astrocytic cells, said method comprising contacting said sample with at least one member selected from the group consisting of protein A, an ion exchange resin and a lectin.

4. The method according to claim 3, wherein the lectin is concanavalin A.

5. A method for assaying, in a biological sample, the toxic activity of a gliotoxic factor having toxic activity with respect to astrocytic

cells, said method comprising: incubating said biological sample in a culture medium containing astrocytes, culturing said astrocytes, and assaying at least one population selected from the group consisting of dead astrocytes and living astrocytes.

6. The method according to claim 5, further comprising: assaying the dead astrocytes with a first colorimetric assay method employing calcein-AM; and assaying the living astrocytes by a second colorimetric assay method employing ethidium homodimer.

7. The method according to claim 5, further comprising assaying the living astrocytes with a colorimetric assay method employing methyltetrazolium bromide.

8. The method according to claim 5, further comprising assaying the dead astrocytes with a radioactive assay method employing ^{51} Cr.

9. The method according to claim 5, wherein the culture medium comprises immortalized astrocytes.

10. A method for assaying, in a biological sample, the toxic activity of a gliotoxic factor having toxic activity with respect to astrocytic cells, said method comprising: incubating said sample in a culture medium comprising astrocytes, culturing said astrocytes, and performing at least one assay from the group consisting of assaying fragmentation of DNA of the astrocytes, assaying cytomorphological disorganization of a network of intermediate filaments, and assaying degradation of proteins of said intermediate filaments.

11. The method according to claim 10, wherein said astrocytes are immortalized.

12. A method for assaying, in a biological sample, a gliotoxic factor having toxic activity with respect to astrocytic cells, said method comprising: obtaining the biological sample to be assayed; contacting the biological sample with a composition comprising a ligand that binds to the gliotoxic factor; and qualitatively or quantitatively assaying an amount of the ligand bound to the gliotoxic factor to qualitatively or quantitatively assay an amount of the gliotoxic factor in said sample.

13. The method according to claim 12, wherein the ligand is a lectin.

14. The method according to claim 13, wherein the lectin is concanavalin A.

15. The method according to claim 12, wherein the ligand is an antibody specific to the gliotoxic factor.

16. The method according to claim 12, wherein the ligand is bound to a solid support.

17. The method according to claim 16, wherein the solid support is a filter.

18. A method for assaying, in a biological sample, a gliotoxic factor having toxic activity with respect to astrocytic cells, said method comprising: loading the biological sample onto a solid support to which a first ligand is bound; binding the gliotoxic factor in the biological sample to the first ligand; washing unbound portions of the biological sample off of the solid support; loading a composition comprising a

second ligand onto the solid support; binding the second ligand to the gliotoxic factor bound to the first ligand bound to the solid support; washing unbound portions of the composition off of the solid support; and qualitatively or quantitatively assaying an amount of the second ligand bound to the gliotoxic factor bound to the first ligand bound to the solid support to qualitatively or quantitatively assay an amount of the gliotoxic factor in said sample.

19. The method according to claim 18, wherein the second ligand comprises a marker.

20. The method according to claim 18, further comprising binding a marker to the second ligand bound to the gliotoxic factor bound to the first ligand bound to the solid support.

L3 ANSWER 15 OF 16 USPATFULL on STN
97:63920 Process and culture medium for the production of cells infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy l' Etoile, France (non-U.S. corporation)
US 5650318 19970722
WO 9320188 19931014
APPLICATION: US 1994-157061 19940202 (8)
WO 1993-FR336 19930402 19940202 PCT 371 date 19940202 PCT 102(e) date
PRIORITY: FR 1992-4322 19920403
FR 1992-13443 19921103
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Process for in vitro production of a culture or cell line infected by a viral strain associated with multiple sclerosis (MS), according to which a body sample is taken from an individual suffering from MS, said sample is cultivated in a culture medium which promotes the growth of infected cells to obtain a culture of primary infected cells, and a sample of the culture of primary cells or of a subculture of the latter is cultivated in series, that is to say by successive passages, in said culture medium to obtain the culture or cell line infected by a virus associated with MS, which comprises a procedure in which the culture medium also contains a beta anti-interferon antibody or an antibody which is directed against an antigenically close molecule, the antibody playing an inhibiting role in viral expression and allowing long-lasting expression and propagation of the viral strain in the culture or cell line.
CLM What is claimed is:
1. A process for the in vitro production of a culture or cell line infected by a viral strain associated with multiple sclerosis (MS), said viral strain having at least one of its replication and expression inhibited by beta-interferon, said process comprising: obtaining a body sample from an individual suffering from MS, cultivating said sample in a culture medium which promotes the growth of infected cells to obtain a culture or cell line of primary infected cells, and cultivating by successive passages a sample of the culture or cell line of primary infected cells or a subculture of said culture or cell line in said culture medium to obtain the culture or cell line infected by a viral strain associated with MS, wherein the culture medium also contains an antibody that recognizes an epitope of beta-interferon, and said culture medium allows persistent expression and propagation of the viral strain in the culture or cell line.

2. The process as claimed in claim 1, wherein the body sample contains infected plexus choroideus cells.

3. A process for the production of a continuous infected culture or cell line comprising cells infected by at least one human viral strain associated with multiple sclerosis (MS) and whose replication is inhibited by beta-interferon, said process comprising the following steps: (a) cultivating human cells infected by said viral strain to obtain at least one primary culture infected by said viral strain, (b) cultivating non-infected human cells permissive to said viral strain to obtain at least one permissive culture, (c) cocultivating at least one sample of the primary infected culture and at least one sample of the permissive culture to obtain a first derived culture infected by said viral strain, (d) cultivating the first derived infected culture in series by steps comprising cocultivation of a new sample of a permissive non-infected culture and a sample of the first derived infected culture or of a subculture of the first derived infected culture to obtain a new subculture of the same first derived infected culture constituting a continuous viral culture in non-immortal cells, at least any one of the culture steps (a) to (d) being carried out with a culture medium comprising an antibody that recognizes an epitope of beta-interferon.

4. The process as claimed in claim 3, wherein said human cells infected by said viral strain comprise at least one member selected from the group consisting of leptomeningeal cells, plexus choroideus cells, myeloid blood cells, and lymphocytes.

5. The process as claimed in claim 3, wherein said noninfected human cells comprise human plexus choroideus cells.

6. The process as claimed in claim 3, wherein said step (a) is carried out a plurality of times to provide a plurality of said primary cultures infected by differing viral strains, and step (c) is carried out by coculture of a sample of the permissive culture and of samples of said plurality of infected primary cultures.

7. A culture medium for carrying out a process as claimed in claim 1, comprising at least one amino acid, at least one vitamin factor, at least one inorganic salt and glucose, which comprises an anti-beta-interferon antibody.

8. A culture medium as claimed in claim 7, which comprises, in addition to the anti-beta-interferon antibody: between 400 and 2250 mg/l of said at least one amino acid, between 3.5 and 130 mg/l of said at least one vitamin factor, between 9100 and 13,000 mg/l of said at least one inorganic salt, and between 1000 and 6000 mg/l of glucose.

9. A biological cell material, which comprises cells sampled from or belonging to a culture or cell line infected by a viral strain associated with multiple sclerosis (MS), obtained by a process as claimed in claim 1, or derived cells obtained by modification of the genome of said cells without alteration of their phenotype.

10. The process as claimed in claim 3, wherein said human cells infected by said viral strain are selected from the group consisting of macrophages and monocytes.

11. A culture medium as claimed in claim 8, further comprising at least one growth factor selected from the group consisting of Endothelial Cell Growth Factor and basic Fibroblast Growth Factor.

12. A process for the production of a viable infected culture or cell line comprising cells infected by multiple sclerosis (MS), said process comprising: (a) cultivating MS infected human cells to obtain at least one culture or cell line of primary infected cells, (b) cultivating non-infected human cells that are permissive to MS to obtain at least one permissive culture, (c) cocultivating at least one sample of the primary infected culture or cell line of primary infected cells and at least one sample of the permissive culture to obtain a first derived infected culture, (d) cultivating the first infected derived culture in series, by cocultivating a new sample of a non-infected permissive culture and a sample of the first infected derived culture or of a subculture of the first infected derived culture to obtain a new subculture of the same first infected derived culture, constituting a viable cell culture or cell line, wherein at least a portion of said process is carried out with a culture medium comprising an antibody that recognizes an epitope of beta-interferon.

13. The process according to claim 12, wherein said infected and non-infected human cells are nervous system cells.

14. The biological cell material as claimed in claim 9, wherein said cell line is cell line PLI-2, deposited at the ECACC on Jul. 22, 1992, under No. 92072201.

L3 ANSWER 16 OF 16 USPATFULL on STN
96:116271 Process for the production of a viable cell culture infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)Universite Joseph Fourier, Grenoble, France (non-U.S. corporation)
US 5585262 19961217
WO 9320189 19931014
APPLICATION: US 1994-157060 19940202 (8)
WO 1993-FR337 19930402 19940202 PCT 371 date 19940202 PCT 102(e) date
PRIORITY: FR 1992-4322 19920403
FR 1992-13447 19921103
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a process for in vitro culture of cells infected by a virus associated with multiple sclerosis and to the infected cell lines thus produced. The process is the cultivation of human cells infected by a viral strain to obtain at least one culture of primary cells infected by the said viral strain, along with the cultivation of non-infected human cells permissive to the viral strain to obtain at least one permissive culture, followed by cocultivation of at least one sample of a culture of infected primary cells and one sample of the permissive culture to obtain a first infected derived culture, then cultivating in series of the first infected derived culture. The invention is used in particular in the pharmaceutical diagnostics industry sector. In the preferred process, the infected cells are leptomeningeal cells and the permissive cells are leptomeningeal cells or plexuschoroideus cells.
CLM What is claimed is:
1. A process for producing a viable cell culture infected by at least one human viral strain associated with multiple sclerosis, said process comprising: (a) cultivating infected leptomeningeal cells to establish a primary culture of cells infected with said viral strain, (b)

cultivating non-infected leptomeningeal cells or plexus choroideus cells to establish a permissive, non-infected culture, (c) cocultivating said infected cells from the primary culture with cells from the permissive culture to obtain a first derived culture of infected leptomeningeal cells or infected plexus choroideus cells; and (d) cocultivating cells from the derived culture with cells from the permissive culture to obtain a subculture of viable infected cells.

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E1            1      OTT BURKHARD/IN
E2            2      OTT C NEIL/IN
E3            0 --> OTT CATHERINE/IN
E4            1      OTT CHARLES D/IN
E5            1      OTT CHARLIE M/IN
E6            1      OTT CHARLOTTE A/IN
E7           12      OTT CHRISTIAN/IN
E8            1      OTT CHRISTIAN G/IN
E9            5      OTT CHRISTOF/IN
E10           3      OTT CHRISTOPHER C/IN
E11           1      OTT CHRISTOPHER M/IN
E12           1      OTT CHRISTOPHER MICHAEL/IN

=> e mandran bernard/in
E1            2      MANDRALIS ZENON I/IN
E2            9      MANDRALIS ZENON IOANNIS/IN
E3            0 --> MANDRAN BERNARD/IN
E4            1      MANDRAND BERBARD/IN
E5            1      MANDRAND BERNAD/IN
E6           41      MANDRAND BERNARD/IN
E7            4      MANDRAND BERNARD F/IN
E8            1      MANDRAND BERNARD FABIEN/IN
E9            1      MANDRAS CHRISTIAN/IN
E10           2      MANDRAS CHRISTIAN MAURICE/IN
E11           1      MANDREA EUGENE/IN
E12           1      MANDRECK COLLIN/IN

=> s e5-e8
              1 "MANDRAND BERNAD"/IN
             41 "MANDRAND BERNARD"/IN
              4 "MANDRAND BERNARD F"/IN
              1 "MANDRAND BERNARD FABIEN"/IN
L4           47 ("MANDRAND BERNAD"/IN OR "MANDRAND BERNARD"/IN OR "MANDRAND
                BERNARD F"/IN OR "MANDRAND BERNARD FABIEN"/IN)

=> d his

     (FILE 'HOME' ENTERED AT 12:06:09 ON 04 APR 2005)

     FILE 'USPATFULL' ENTERED AT 12:06:16 ON 04 APR 2005
                E PARANHOS-BACCALA G/IN
L1           12 S E2
                E PERRON HERVE/IN
L2           22 S E3
L3           16 S L2 NOT L1
                E OTT CATHERINE/IN
                E MANDRAN BERNARD/IN
L4           47 S E5-E8
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=> s l4 not (l1 or l2)
L5 30 L4 NOT (L1 OR L2)

=> d l5,cbib,1-30

L5 ANSWER 1 OF 30 USPATFULL on STN
2005:81491 RNA-dependent RNA polymerase functioning preferably on a RNA matrix and promoter-dependent transcription process with said RNA-dependent RNA polymerase.
Cheynet-Sauvion, Valerie, Verin, FRANCE
Arnaud-Barbe, Nadege, Saint Sorlin, FRANCE
Oriol, Guy, Saint Chamond, FRANCE
McAllister, William, Perth Amboy, NJ, UNITED STATES
Mandrand, Bernard, Villeurbanne, FRANCE
Mallet, Francois, Villeurbanne, FRANCE
BIO MERIEUX, Marcy L'Etoile, FRANCE (non-U.S. corporation)
US 2005069933 A1 20050331
APPLICATION: US 2004-940964 A1 20040915 (10)
PRIORITY: FR 1997-4166 19970404
DOCUMENT TYPE: Utility; APPLICATION.

L5 ANSWER 2 OF 30 USPATFULL on STN
2005:65130 Composite nanospheres and their conjugates with biomolecules.
Mondain-Monval, Olivier, Bordeaux, FRANCE
Elaissari, Abdelhamid, Lyons, FRANCE
Bosc, Eric, Salles, FRANCE
Pichot, Christian, Corbas, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Bibette, Jerome, Bordeaux, FRANCE
Bio Merieux, Marcy l'Etoile, FRANCE (non-U.S. corporation)Centre National de la Recherche Scientifique, Paris, FRANCE (non-U.S. corporation)
US 6866838 B1 20050315
WO 2001033223 20010510
APPLICATION: US 2002-129141 20020729 (10)
WO 2000-FR3085 20001106 20020729 PCT 371 date
PRIORITY: FR 1999-14194 19991105
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 30 USPATFULL on STN
2005:44501 Bi-functionalised metallocenes use for marking biological molecules.
Chaix-Bauvais, Carole, Chaponnay, FRANCE
Moustrou, Corinne, Marseille, FRANCE
Navarro, Aude-Emmanuelle, Marseille, FRANCE
Brisset, Hugues, Saint Cyr Sur Mer, FRANCE
Garnier, Francis, Champigny Sur Marne, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Spinelli, Nicolas, Lyon, FRANCE
BIO MERIEUX (non-U.S. corporation)
US 2005038234 A1 20050217
APPLICATION: US 2004-501347 A1 20041013 (10)
WO 2003-FR484 20030214
PRIORITY: FR 2002-1858 20020214
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 4 OF 30 USPATFULL on STN
2004:299124 Method for detecting at a solid support of complexing or hybridization between at least two basic molecules based on an amplified signal at the support.

Garnier, Francis, Champigny-sur-Marne, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
US 2004234991 A1 20041125
APPLICATION: US 2004-485328 A1 20040128 (10)
WO 2002-FR2781 20020801
PRIORITY: FR 2001-10302 20010801
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 30 USPATFULL on STN
2004:220989 Method for depositing a spot product of a product of interest, and use for isolating and/or determining an analyte.
Perrin, Agnes, Lyon, FRANCE
Theretz, Alain, Ecully, FRANCE
Delair, Thierry, Echalas, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
US 2004170757 A1 20040902
APPLICATION: US 2004-475873 A1 20040427 (10)
WO 2002-FR1444 20020425
PRIORITY: FR 2001-5639 20010426
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 6 OF 30 USPATFULL on STN
2004:142825 Valves activated by electrically active polymers or by shape-memory materials, device containing same and method for using same.
Garnier, Francis, Champigny sur Marne, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Broyer, Patrick, Villeurbanne, FRANCE
Imbaud, Pierre, Pommiers, FRANCE
US 2004108479 A1 20040610
APPLICATION: US 2003-433261 A1 20031125 (10)
WO 2001-FR3783 20011130
PRIORITY: FR 2000-15550 20001201
DOCUMENT TYPE: Utility; APPLICATION.

L5 ANSWER 7 OF 30 USPATFULL on STN
2004:120046 Biocompatible polymer for fixing biological ligands.
Charreyre, Marie-Therese, Lyon, FRANCE
D'Agosto, Franck, Dijon, FRANCE
Favier, Arnaud, Marsonnas, FRANCE
Pichot, Christian, Corbas, FRANCE
Mandrand, Bernad, Villeurbanne, FRANCE
US 2004091451 A1 20040513
APPLICATION: US 2003-296889 A1 20030127 (10)
WO 2001-FR1663 20010529
PRIORITY: FR 2000-6861 20000529
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 8 OF 30 USPATFULL on STN
2003:250905 Method for isolating proteins or protein and nucleic acid associations, or particle and protein complexes, reagent and uses.
Elaissari, Abdelhamid, Lyon, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Delair, Thierry, Echalas, FRANCE
Spencer, Doran, Eureka, CA, UNITED STATES
Arkis, Ahmed, Lyon, FRANCE
US 2003175691 A1 20030918
APPLICATION: US 2003-182126 A1 20030113 (10)

WO 2001-FR205 20010122
PRIORITY: FR 2000-862 20000121
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 9 OF 30 USPATFULL on STN
2003:187416 Mutated hepatitis b virus, its nucleic and protein constituents and uses thereof.
Trepo, Christian, Bron, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Kay, Alan, Lyon, FRANCE
Chemin, Isabelle, Caluire, FRANCE
Komurian-Pradel, Florence, Poleymieux au Mont D'Or, FRANCE
US 2003129202 A1 20030710
APPLICATION: US 2002-169668 A1 20021216 (10)
WO 2001-FR38 20010105
PRIORITY: FR 2000-129 20000106
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 10 OF 30 USPATFULL on STN
2003:47587 Magnetic particles, method for obtaining same and uses for separating molecules.
Elaissari, Abdelhamid, Lyons, FRANCE
Pichot, Christian, Corbas, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Bio Merieux, Marcy l'Etoile, FRANCE (non-U.S. corporation)
US 6521341 B1 20030218
WO 9935500 19990715
APPLICATION: US 2000-582352 20000921 (9)
WO 1999-FR11 19990106
PRIORITY: FR 1998-220 19980106
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 11 OF 30 USPATFULL on STN
2002:280062 Saturated and unsaturated abietane derivatives, derived conjugates and uses in a diagnostic composition, a reagent and a device.
Charles, Marie Helene, Condrieu, FRANCE
Piga, Nadia, Ecully, FRANCE
Battail-Poirot, Nicole, Lyon, FRANCE
Veron, Laurent, Lyon, FRANCE
Delair, Thierry, Echalas, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
US 2002155496 A1 20021024
APPLICATION: US 2001-771554 A1 20010130 (9)
PRIORITY: FR 1998-10084 19980731
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 12 OF 30 USPATFULL on STN
2002:221310 RNA-DEPENDENT RNA POLYMERASE FUNCTIONING PREFERABLY ON RNA MATRIX AND PROMOTER-DEPENDENT TRANSCRIPTION PROCESS WITH SAID RNA- DEPENDENT RNA POLYMERASE.
CHEYNET-SAUVION, VALERIE, VERIN, FRANCE
ARNAUD-BARBE, NADEGE, SAINT SORLIN, FRANCE
ORIOL, GUY, SAINT CHAMOND, FRANCE
MCALLISTER, WILLIAM, PERTH AMBOY, NJ, UNITED STATES
MANDRAND, BERNARD, VILLEURBANNE, FRANCE
MALLET, FRANCOIS, VILLEURBANNE, FRANCE

US 2002119449 A1 20020829
APPLICATION: US 1999-402131 A1 19991208 (9)
WO 1998-FR635 19980327
PRIORITY: FR 1997-4166 19970404
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 13 OF 30 USPATFULL on STN
2002:105978 COMPLEX CHEMICAL COMPOUND, SYNTHESIS AND VARIOUS APPLICATIONS OF SAID COMPOUND.
MINARD, CLAIRE, LYON, FRANCE
CHAIX, CAROLE, BRIGNAIS, FRANCE
DELAIR, THIERRY, ECHALAS, FRANCE
MANDRAND, BERNARD, VILLEURBANNE, FRANCE
US 2002055185 A1 20020509
APPLICATION: US 2000-485154 A1 20000204 (9)
WO 1998-FR1731 19980803
PRIORITY: FR 1997-10300 19970807
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 14 OF 30 USPATFULL on STN
2002:19220 Method for isolating, in particular for detecting or quantifying an analyte in a medium.
Perrin, Agnes, Lyons, FRANCE
Theretz, Alain, Ecully, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Bio Merieux, Marcy l'Etoile, FRANCE (non-U.S. corporation)
US 6342396 B1 20020129
WO 9834116 19980806
APPLICATION: US 1999-355246 19990917 (9)
WO 1998-FR182 19980130 19990917 PCT 371 date
PRIORITY: FR 1997-1313 19970130
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 15 OF 30 USPATFULL on STN
2000:138137 Superparamagnetic monodisperse particles.
Elaissari, Abdelhamid, Lyons, France
Pichot, Christian, Corbas, France
Mandrand, Bernard, Villeurbanne, France
Sauzedde, Florence, Lyons, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6133047 20001017
WO 9745202 19971204
APPLICATION: US 1998-983040 19980115 (8)
WO 1997-FR912 19970523 19980115 PCT 371 date 19980115 PCT 102(e) date
PRIORITY: FR 1996-6765 19960524
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 16 OF 30 USPATFULL on STN
2000:27749 Nucleotide sequence detection with signal amplification.
Delair, Thierry, Echalas, France
Elaissari, Abdelhamid, Lyons, France
Charles, Marie-Helene, Condrieu, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6033853 20000307
WO 9735031 19970925

APPLICATION: US 1997-952397 19970108 (8)
WO 1997-FR483 19970319 19980108 PCT 371 date 19980108 PCT 102(e) date
PRIORITY: FR 1996-3412 19960319
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 17 OF 30 USPATFULL on STN
2000:9697 Reagent and method for the detection of a nucleotide sequence with signal amplification.
Mandrand, Bernard, Villeurbanne, France
Cros, Philippe, Lyons, France
Delair, Thierry, Lyons, France
Charles, Marie-Helene, Condrieu, France
Erout, Marie-Noelle, Sainte Foy les Lyon, France
Pichot, Christian, Corbas, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 6017707 20000125
APPLICATION: US 1997-870730 19970606 (8)
PRIORITY: FR 1993-11006 19930915
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 18 OF 30 USPATFULL on STN
1999:149303 Freeze valve and treatment enclosure controlled by at least one such valve.
Colin, Bruno, Marcy L'Etoile, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5988197 19991123
APPLICATION: US 1996-598607 19960212 (8)
PRIORITY: FR 1995-1802 19950213
FR 1995-2541 19950228
DOCUMENT TYPE: Utility; Granted.

L5 ANSWER 19 OF 30 USPATFULL on STN
1999:136938 System of probes enabling HLA-DR typing to be performed, and typing method using said probes.
Allibert, Patrice Andre, Grezieu La Varenne, France
Cros, Philippe, Lyons, France
Mach, Bernard Francois, Geneva, Switzerland
Mandrand, Bernard Fabien, Villeurbanne, France
Tiercy, Jean-Marie, Geneva, Switzerland
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5976789 19991102
APPLICATION: US 1995-485133 19950607 (8)
PRIORITY: FR 1991-9058 19910717
WO 1992-FR702 19920717
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 20 OF 30 USPATFULL on STN
1999:56418 Assembly for treating a sample in a liquid medium, in particular a biological material.
Colin, Bruno, Marcy l'Etoile, France
Mandrand, Bernard, Villeurbanne, France
Imbaud, Pierre, Pommiers, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5902746 19990511
WO 9715815 19970501
APPLICATION: US 1997-849515 19970609 (8)

WO 1996-FR1635 19961018 19970609 PCT 371 date 19970609 PCT 102(e) date
PRIORITY: FR 1995-12669 19951023
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 21 OF 30 USPATFULL on STN
1998:128109 Method for amplifying nucleic acid sequences by strand displacement using DNA/RNA chimeric primers.
Cleuziat, Philippe, Lyons, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy-L'Etoile, France (non-U.S. corporation)
US 5824517 19981020
WO 9704126 19970206
APPLICATION: US 1997-817035 19970516 (8)
WO 1996-FR1166 19960724 19970516 PCT 371 date 19970516 PCT 102(e) date
PRIORITY: FR 1995-8945 19950724
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 22 OF 30 USPATFULL on STN
1998:122221 RNA amplification method requiring only one manipulation step.
Mallet, Francois, Villeurbanne, France
Oriol, Guy, Saint-Chamond, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5817465 19981006
APPLICATION: US 1997-825617 19970331 (8)
PRIORITY: FR 1992-5322 19920429
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 23 OF 30 USPATFULL on STN
1998:61781 Water-soluble compounds derived from a homopolymer or copolymer of maleic anhydride, and applications of the said compounds to supporting biological molecules.
Charles, Marie-Helene, Condrieu, France
Delair, Thierry, Lyons, France
Jaubert, Monique, Craponne, France
Mandrand, Bernard F., Villeurbanne, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5760166 19980602
APPLICATION: US 1996-597455 19960202 (8)
PRIORITY: FR 1992-3425 19920317
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 24 OF 30 USPATFULL on STN
1998:22106 Device for the capture of target molecules, and capturing process using the device.
Mabilat, Claude, Villeurbanne, France
Cros, Philippe, Lyons, France
Mandrand, Bernard, Villeurbanne, France
Charles, Marie-Helene, Condrieu, France
Erout, Marie-Noelle, Sainte Foy les Lyon, France
Pichot, Christian, Corbas, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 5723344 19980303
APPLICATION: US 1994-264996 19940624 (8)
PRIORITY: FR 1993-7797 19930625
DOCUMENT TYPE: Utility; Granted.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 25 OF 30 USPATFULL on STN
97:115102 Reagent and method for the detection of a nucleotide sequence with signal amplification.
Mandrand, Bernard, Villeurbanne, France
Cros, Philippe, Lyons, France
Delair, Thierry, Lyons, France
Charles, Marie-Helene, Condrieu, France
Erout, Marie-Noelle, Saint Foy les Lyon, France
Pichot, Christian, Corbas, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5695936 19971209
WO 9508000 19950323
APPLICATION: US 1995-433505 19950614 (8)
WO 1994-FR1084 19940915 19950614 PCT 371 date 19950614 PCT 102(e) date
PRIORITY: FR 1993-11006 19930915
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 26 OF 30 USPATFULL on STN
97:115092 Sandwich hybridization assays using very short capture probes noncovalently bound to a hydrophobic support.
Cros, Philippe, Lyons, France
Allibert, Patrice, Grezieu la Varenne, France
Mallet, Fran.cedilla.ois, Villeurbanne, France
Mabilat, Claude, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy-L'Etoile, France (non-U.S. corporation)
US 5695926 19971209
APPLICATION: US 1994-255892 19940607 (8)
PRIORITY: FR 1990-7249 19900611
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 27 OF 30 USPATFULL on STN
97:68317 RNA amplification method requiring only one manipulation step.
Mallet, Fran.cedilla.ois, Villeurbanne, France
Oriol, Guy, Saint-Chamond, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5654143 19970805
APPLICATION: US 1995-412229 19950327 (8)
PRIORITY: FR 1992-5322 19920429
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 28 OF 30 USPATFULL on STN
96:33862 Process for immobilizing a nucleic acid fragment by passive attachment to a solid substrate, the solid substrate thus obtained, and its use.
Cros, Philippe, Lyons, France
Allibert, Patrice A., Grezieu la Varenne, France
Mandrand, Bernard F., Villeurbanne, France
Dalbon, Pascal T., Venissieux, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 5510084 19960423
APPLICATION: US 1994-273776 19940712 (8)
PRIORITY: FR 1991-9057 19910717
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 29 OF 30 USPATFULL on STN
96:11197 Water-soluble compounds derived from homopolymer or copolymer of maleic anhydride, and applications of the said compounds to supporting biological molecules.
Charles, Marie-Helene, Condrieu, France
Delair, Thierry, Lyon, France
Jaubert, Monique, Craponne, France
Mandrand, Bernard F., Villeurbanne, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 5489653 19960206
APPLICATION: US 1993-32027 19930316 (8)
PRIORITY: FR 1992-3425 19920317
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 30 OF 30 USPATFULL on STN
95:71422 Water-soluble compounds derived from a homopolymer or copolymer of maleic anhydride, and applications of the said compounds to supporting biological molecules.
Charles, Marie-Helene, Condrieu, France
Delair, Thierry, Lyons, France
Jaubert, Monique, Craponne, France
Mandrand, Bernard F., Villeurbanne, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5439972 19950808
APPLICATION: US 1994-321447 19941012 (8)
PRIORITY: FR 1992-3425 19920317
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 12:06:09 ON 04 APR 2005)

FILE 'USPATFULL' ENTERED AT 12:06:16 ON 04 APR 2005
E PARANHOS-BACCALA G/IN
L1 12 S E2
E PERRON HERVE/IN
L2 22 S E3
L3 16 S L2 NOT L1
E OTT CATHERINE/IN
E MANDRAN BERNARD/IN
L4 47 S E5-E8
L5 30 S L4 NOT (L1 OR L2)

=> file wpids

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	142.92	143.13

FILE 'WPIDS' ENTERED AT 12:15:25 ON 04 APR 2005
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FILE LAST UPDATED: 1 APR 2005 <20050401/UP>
MOST RECENT DERWENT UPDATE: 200521 <200521/DW>
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    FOR DETAILS. <<<

=> e paranhos baccala g/in
E1            1     PARANHOS B C/IN
E2            4     PARANHOS B G/IN
E3           11 --> PARANHOS BACCALA G/IN
E4            3     PARANHOS JUNIOR A/IN
E5            1     PARANHOS MONTENEGRO F/IN
E6            1     PARANHOSBACCALA G/IN
E7            1     PARANICAS P C/IN
E8            3     PARANICH A V/IN
E9            1     PARANICHEV V N/IN
E10           2     PARANIN A A/IN
E11           1     PARANIN L N/IN
E12           1     PARANIN R Y U/IN

=> s e3
L6           11 "PARANHOS BACCALA G"/IN

=> d l6,bib,ab,1-11

L6   ANSWER 1 OF 11  WPIDS  COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN   2004-071561 [07]   WPIDS
DNC  C2004-029611
TI   In vitro culture of hepatitis C virus, useful as diagnostic reagents and
     in screening for antivirals, uses host cells able to synthesize and
     secrete lipoproteins.
DC   B04 D16
IN   ANDRE, P; KOMURIAN, P F; LOTTEAU, V; PARNAHOS, B G; KOMURIAN-PRADEL, F;
     PARANHOS-BACCALA, G
PA   (INMR) BIO MERIEUX; (INRM) INSERM INST NAT SANTE & RECH MEDICALE; (INMR)
     BIOMERIEUX SA
CYC  105
PI   WO 2003106665   A1 20031224 (200407)* FR   30
        RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
            LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH
            PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN
            YU ZA ZM ZW
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FR 2840921 A1 20031219 (200410)
AU 2003260593 A1 20031231 (200451)
EP 1513930 A1 20050316 (200519) FR
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

ADT WO 2003106665 A1 WO 2003-FR1820 20030616; FR 2840921 A1 FR 2002-7600 20020618; AU 2003260593 A1 AU 2003-260593 20030616; EP 1513930 A1 EP 2003-760045 20030616, WO 2003-FR1820 20030616

FDT AU 2003260593 A1 Based on WO 2003106665; EP 1513930 A1 Based on WO 2003106665

PRAI FR 2002-7600 20020618

AB WO2003106665 A UPAB: 20040128
NOVELTY - A method for in vitro culture of hepatitis C virus (HCV) comprises contacting particles (A), containing the RNA of HCV, with cells that can synthesize and secrete lipoproteins (LP), in a culture medium that promotes synthesis and secretion of LP, then harvesting the virus produced, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a method of screening and/or selecting antiviral agents (I) by adding test compounds to the medium during the new in vitro culture method; and

(2) therapeutic composition that can affect, qualitatively or quantitatively, propagation or replication of HCV in vivo, containing an agent (Ia) able to modulate, repress or inhibit synthesis of LP.

ACTIVITY - Virucide; Hepatotropic; Antiinflammatory.

No biological data given.

MECHANISM OF ACTION - Inhibition of lipoprotein synthesis.

USE - The virus produced by the new method is useful diagnostically as a source of antigen; and the cultured cells can be used to screen for antiviral agents. Agents that modulate, repress or inhibit synthesis of lipoproteins can be used to reduce propagation and replication of HCV in vivo.

ADVANTAGE - Replication of viral particles is improved by using cells able to synthesize LP.

Dwg.0/3

L6 ANSWER 2 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2004-032461 [03] WPIDS
CR 1998-322732 [28]; 2003-512253 [48]
DNC C2004-010886
TI New isolated nucleic acid and their fragments having the pol gene of a retrovirus, useful for diagnosing, preventing and/or treating multiple sclerosis and/or rheumatoid arthritis.
DC A89 B04 D16
IN BEDIN, F; BESEME, F; GARSON, J A; JOLIVET-REYNAUD, C; KOMURIAN-PRADEL, F; MANDRAND, B; **PARANHOS-BACCALA, G**; PERRON, H; TUKE, P W
PA (INMR) BIO MERIEUX
CYC 1
PI US 2003198647 A1 20031023 (200403)* 193
ADT US 2003198647 A1 CIP of US 1996-756429 19961126, Div ex US 1997-979847 19971126, US 2002-114104 20020403
PRAI US 1997-979847 19971126; US 1996-756429 19961126; US 2002-114104 20020403
AB US2003198647 A UPAB: 20040112
NOVELTY - An isolated nucleic acid comprises the pol gene of a retrovirus associated with multiple sclerosis or rheumatoid arthritis.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a nucleotide fragment comprising:

(a) a coding sequence consisting of a fully defined sequence of 2304 or 2365 bp (SEQ. ID. NO: 87 and 88), or their complements, and sequences encoding the peptide sequence having a fully defined sequence of 768 amino acids (SEQ. ID NO: 89); or

(b) a portion of the coding nucleotide sequence, which encodes a peptide that is recognized by sera of patients infected with the multiple sclerosis retrovirus-1 (MSRV-1) virus;

(2) a process for detecting, in a biological sample, a virus associated with multiple sclerosis or rheumatoid arthritis, comprising contacting the nucleotide fragment of (1) with the biological sample, and determining whether the fragment hybridizes with a nucleic acid sequence in the biological sample, where hybridization indicates the presence of the virus;

(3) a nucleic acid probe for the detection of a virus associated with multiple sclerosis or rheumatoid arthritis, where the probe specifically hybridizes with the nucleotide fragment of (1);

(4) a primer for the amplification by polymerization of a nucleic acid of a viral material associated with multiple sclerosis or rheumatoid arthritis, comprising a nucleotide sequence having, for any succession of at least 20 contiguous monomers, at least 70% homology with the nucleotide sequence of the fragment of (1);

(5) an isolated or purified polypeptide encoded by an open reading frame of the nucleotide sequence of the fragment of (1);

(6) an isolated or purified polypeptide comprising a fully defined peptide sequence of 114, 654 or 149 amino acids (SEQ. ID NO: 90, 91 and 92), given in the specification, a polypeptide encoded by an open reading frame beginning at nucleotide 18, 341 and 1858, and ending at nucleotide 340, 2304 and 2304, respectively, and an equivalent polypeptide which exhibits the proteolytic, transcriptase or ribonuclease activity of a polypeptide with amino acid SEQ. ID NO: 90, 91 and 92, respectively; and

(7) a polypeptide having amino acid SEQ. ID NO: 89.

ACTIVITY - Neuroprotective; Antirheumatic; Antiarthritic.

No biological data given.

MECHANISM OF ACTION - Gene-Therapy.

USE - The methods and compositions of the present invention are useful for diagnosing, preventing and/or treating multiple sclerosis and/or rheumatoid arthritis.

Dwg.0/53

L6 ANSWER 3 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2003-512253 [48] WPIDS
CR 1998-322732 [28]; 2004-032461 [03]
DNC C2003-137124
TI New isolated or purified nucleic acid associated with multiple sclerosis and/or rheumatoid arthritis, useful for detecting a virus associated with multiple sclerosis or rheumatoid arthritis in a biological sample.
DC B04 D16
IN BEDIN, F; BESEME, F; GARSON, J A; JOLIVET-REYNAUD, C; KOMURIAN-PRADEL, F; MANDRAND, B; **PARANHOS-BACCALA, G**; PERRON, H; TUKE, P W
PA (BEDI-I) BEDIN F; (BESE-I) BESEME F; (GARS-I) GARSON J A; (JOLI-I) JOLIVET-REYNAUD C; (KOMU-I) KOMURIAN-PRADEL F; (MAND-I) MANDRAND B; (PARA-I) PARANHOS-BACCALA G; (PERR-I) PERRON H; (TUKE-I) TUKE P W; (INMR) BIO MERIEUX
CYC 1
PI US 2003039664 A1 20030227 (200348)* 193
US 6582703 B2 20030624 (200349)
ADT US 2003039664 A1 CIP of US 1996-756429 19961126, US 1997-979847 19971126; US 6582703 B2 CIP of US 1996-756429 19961126, US 1997-979847 19971126
PRAI US 1997-979847 19971126; US 1996-756429 19961126

AB US2003039664 A UPAB: 20040112

NOVELTY - An isolated or purified nucleic acid associated with multiple sclerosis and/or rheumatoid arthritis, is new.

DETAILED DESCRIPTION - The isolated or purified nucleic acid associated with multiple sclerosis and/or rheumatoid arthritis:

(a) comprises a sequence of 23 or 24 bp, or a sequence selected from 8 sequences encoding an 8-amino acid sequence bp (designated S1-S8, respectively) given in the specification e.g. Pro-Thr-Ser-Gln-Leu-Thr-Trp-Thr, their equivalents or complements, excluding HSERV-9 sequences;

(b) encodes a polypeptide displaying, for any contiguous succession of at least 30 amino acids, at least 70% homology with a peptide encoded by a sequence selected from S1-S8, or their complements;

(c) comprises the pol gene of an isolated retrovirus associated with multiple sclerosis or rheumatoid arthritis, or its equivalents; or

(d) comprises the pol gene of an isolated virus encoding a reverse transcriptase comprising an enzymatic site between amino acid domains LPQG and YXDD, where the virus has a phylogenetic distance from HSERV-0 of 0.063 plus or minus 0.1, or its equivalent sequences.

INDEPENDENT CLAIMS are also included for the following:

(1) a nucleotide fragment comprising:

(a) a sequence selected from S1-S8, their complements or equivalents, where the group excludes a sequence of 1158 bp, and the fragment does not comprise the sequence HSERV-9; or

(b) a coding nucleotide sequence, or its equivalent sequence or portion, comprising S1-S8, their complements, or sequences encoding peptide having a sequence encoded by a sequence of 85 bp given in the specification or a sequence selected from 8 sequences each consisting of 8 amino acids (designated P1-P8), where the coding nucleotide sequence encodes a peptide that is recognized by a sera of patients infected with the MSRV-1 virus, and/or in whom the MSRV-1 virus has been reactivated;

(2) a process for detecting a virus associated with multiple sclerosis or rheumatoid arthritis in a biological sample;

(3) a nucleic acid probe for the detection of a virus associated with multiple sclerosis or rheumatoid arthritis, where the probe specifically hybridizes with the nucleotide fragment of (1);

(4) a primer for the amplification by polymerization of a nucleic acid of a viral material associated with multiple sclerosis or rheumatoid arthritis, comprising a nucleotide sequence having, for any succession of at least 20 contiguous monomers, at least 70% homology with the nucleotide sequence fragment above;

(5) an isolated and purified polypeptide encoded by an open reading frame (ORF) of the nucleotide sequence of the nucleotide sequence fragment defined above, or comprising a peptide sequence encoded by a 25 (A1), 25 (A2) or 26 (A3) bp sequence given in the specification;

(6) a polypeptide encoded by an ORF consisting of a first, second and third ORF at nucleotides 18-340, nucleotides 341-2304, and nucleotides 1858-2304 of S1, respectively;

(7) a polypeptide exhibiting an inhibitory activity on the proteolytic, reverse transcriptase or ribonuclease H activity of the polypeptide of (6);

(8) an isolated or purified polypeptide encoded by an ORF of the nucleotide sequence of the fragment above;

(9) an isolated or purified (antigenic) polypeptide comprising P1-P8 or their equivalent sequences, where the antigenic polypeptide is recognized by a sera of patients infected with the MSRV-1 virus, and/or in whom the MSRV-1 virus has been reactivated;

(10) a process for detecting in a biological sample, the presence of or exposure to a virus associated with multiple sclerosis or rheumatoid arthritis; and

(11) an antibody directed against the MSRV-1 virus obtained by

immunologically reacting a human or animal body or cells with an immunogenic agent consisting of the antigenic polypeptide defined above.

USE - The nucleic acids are useful for detecting a biological sample a virus associated with multiple sclerosis or rheumatoid arthritis, or for detecting in a biological sample, the presence of or exposure to a virus associated with multiple sclerosis or rheumatoid arthritis.

Dwg.0/53

L6 ANSWER 4 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2002-156795 [21] WPIDS
DNN N2002-119334 DNC C2002-049038
TI Complex of lipo-viral particles and immunoglobulins, useful for in vitro culture of hepatitis C virus and for diagnosis, vaccination and drug screening.
DC B04 D16 S03
IN ANDRE, P; KOMURIAN, P F; LOTTEAU, V; PARANHOS, B G; KOMURIAN-PRADEL, F; **PARANHOS-BACCALA, G**
PA (INMR) BIO MERIEUX; (INRM) INSERM INST NAT SANTE & RECH MEDICALE; (INRM) INST NAT SANTE & RECH MEDICALE
CYC 97
PI FR 2812304 A1 20020201 (200221)* 26
WO 2002010353 A1 20020207 (200221) FR
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
US 2002058044 A1 20020516 (200237)
AU 2001082251 A 20020213 (200238)
US 6548295 B2 20030415 (200329)
EP 1305402 A1 20030502 (200331) FR
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
JP 2004504836 W 20040219 (200414) 56
ADT FR 2812304 A1 FR 2000-10085 20000731; WO 2002010353 A1 WO 2001-FR2507 20010731; US 2002058044 A1 US 2001-917915 20010731; AU 2001082251 A AU 2001-82251 20010731; US 6548295 B2 US 2001-917915 20010731; EP 1305402 A1 EP 2001-960853 20010731, WO 2001-FR2507 20010731; JP 2004504836 W WO 2001-FR2507 20010731, JP 2002-516071 20010731
FDT AU 2001082251 A Based on WO 2002010353; EP 1305402 A1 Based on WO 2002010353; JP 2004504836 W Based on WO 2002010353
PRAI FR 2000-10085 20000731
AB FR 2812304 A UPAB: 20020403

NOVELTY - A complex (A) comprising lipo-viral particles (LPVs) and associated human immunoglobulins (Ig), and with density below 1.063 g/ml, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparing (A) from the plasma or serum of a patient infected with hepatitis C virus (HCV);

in vitro culture of HCV by growing permissive cells in presence of (A);

(2) preparing a composition (B) for detecting anti-HCV antibodies (Ab) by (partial) purification of (A) or of polypeptides (I) obtained by method (1);

(3) preparing Ab, or its fragments, by immunization with (A) or (I);

(4) diagnostic composition or kit, comprising at least (A), (I) or Ab, or fragments;

(5) vaccines containing at least (A) or (I); and

(6) screening/selecting antiviral agents using a cell line produced by method (1).

ACTIVITY - Virucide; hepatotropic; antiinflammatory.

MECHANISM OF ACTION - Vaccine. No supporting data is given.

USE - (A) are used:

(a) for in vitro culture of hepatitis C virus (HCV) and production of associated polypeptides (I);

(b) for detecting antibodies (Ab) directed against HCV; and

(c) to raise Ab.

(A), (I) and Ab (or their fragments) are used for diagnosis and (A) or (I) also in vaccines. The cell lines used for in vitro culture of HCV are used to screen for antiviral agents, also for studying mechanisms of viral replication and for testing neutralizing antibodies or antiviral agents.

Dwg.0/1

L6 ANSWER 5 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2001-168702 [17] WPIDS
DNC C2001-050427
TI In vitro propagation of Toga or Flavi viruses, useful e.g. for producing vaccines or diagnostic agents, by culture in permissive cells in presence of unsaturated fatty acid.
DC B04 D16
IN ANDRE, P; KOMURIAN, P F; LOTTEAU, V; PARANHOS, B G; KOMURIAN-PRADEL, F; **PARANHOS-BACCALA, G**
PA (INMR) BIO MERIEUX; (INRM) INSERM INST NAT SANTE & RECH MEDICALE; (INRM) INST NAT SANTE & RECH MEDICALE
CYC 95
PI WO 2001009289 A1 20010208 (200117)* FR 41
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
FR 2796962 A1 20010202 (200117)
AU 2000068474 A 20010219 (200129)
EP 1203076 A1 20020508 (200238) FR
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2003506031 W 20030218 (200315) 38
US 2004229336 A1 20041118 (200477)
ADT WO 2001009289 A1 WO 2000-FR2202 20000731; FR 2796962 A1 FR 1999-10095 19990730; AU 2000068474 A AU 2000-68474 20000731; EP 1203076 A1 EP 2000-956580 20000731, WO 2000-FR2202 20000731; JP 2003506031 W WO 2000-FR2202 20000731, JP 2001-514083 20000731; US 2004229336 A1 Cont of WO 2000-FR2202 20000731, Cont of US 2002-31439 20020225, US 2004-776617 20040212
FDT AU 2000068474 A Based on WO 2001009289; EP 1203076 A1 Based on WO 2001009289; JP 2003506031 W Based on WO 2001009289
PRAI FR 1999-10095 19990730
AB WO 200109289 A UPAB: 20010328
NOVELTY - In vitro culture, propagation and replication of viruses (I) of the Togaviridae or Flaviviridae families comprises culturing a fraction of lipid-viral particles (LPV), from the serum or plasma of an infected patient with permissive cells that have an endocytotic pathway mediated by a lipoprotein receptor and modulated by an activator, i.e. at least one 16-20C unsaturated fatty acid, or its derivative.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) culture medium for the process comprising Dulbecco's modified Eagle medium, supplemented by 0-10 mM sodium pyruvate, 0-10% non-essential amino acids, 1-10 mM glutamine, 100-200 units/ml penicillin, 100-200 mg/ml streptomycin, 1-20% calf serum and 0.1-5% bovine serum albumin or human serum albumin coupled to a fatty acid;

(2) preparing a composition for detecting (I)-specific antibodies by (partial) purification of viral particles, or their polypeptides, (VP) produced by the new method;

(3) preparation of antibodies, or their fragments, (Ab) directed against (I) by immunization with VP;

(4) diagnostic composition containing VP or Ab;

(5) diagnostic kit containing the composition of (4);

(6) vaccine composition containing VP, optionally with vehicle, excipient and/or adjuvant;

(7) therapeutic composition comprising a ligand that can modulate, repress or inhibit the specified endocytotic pathway; and

(8) method for screening and/or selecting antiviral agents by treating an infected cell line with test compounds.

ACTIVITY - Antiviral.

No biological data.

MECHANISM OF ACTION - Vaccine.

USE - Viral particles, or their polypeptides, produced by the method are used for diagnostic detection of (I)-specific antibodies, e.g. in diseases carriers, to generate (I)-specific antibodies (Ab) for use in diagnosis, and in vaccines, especially where (I) is the hepatitis C or G virus.

Ligands that modify the specified endocytotic pathway are used for treatment of viral infections and the cultured cells can be used to study viral replication and to screen for therapeutic antibodies and antiviral agents.

ADVANTAGE - Supplementing the culture with a fatty acid facilitates entry of virus into cells.

Dwg.0/1

L6 ANSWER 6 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2000-506097 [45] WPIDS
DNN N2000-374240 DNC C2000-151974
TI Nucleotide fragment of LTR-RU5 region from Multiple Sclerosis retrovirus (MSRV) used to detect the presence of MSRV-1 retrovirus in a biological sample.
DC B04 D16 S03
IN BACCALA-PARANHOS, G; KOMURIAN-PRADEL, F; PERRON, H; **PARANHOS-BACCALA, G**
PA (INMR) BIO MERIEUX
CYC 91
PI WO 2000047745 A1 20000817 (200045)* EN 23
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
EP 1029917 A1 20000823 (200046) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
AU 2000024566 A 20000829 (200062)
EP 1151108 A1 20011107 (200168) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

RO SE SI
JP 2002536019 W 20021029 (200274) 27
US 2004043381 A1 20040304 (200417)
ADT WO 2000047745 A1 WO 2000-IB159 20000215; EP 1029917 A1 EP 1999-420041 19990215; AU 2000024566 A AU 2000-24566 20000215; EP 1151108 A1 EP 2000-902825 20000215, WO 2000-IB159 20000215; JP 2002536019 W JP 2000-598643 20000215, WO 2000-IB159 20000215; US 2004043381 A1 Cont of WO 2000-IB159 20000215, Cont of US 2001-890340 20010730, US 2003-637565 20030811
FDT AU 2000024566 A Based on WO 2000047745; EP 1151108 A1 Based on WO 2000047745; JP 2002536019 W Based on WO 2000047745
PRAI EP 1999-420041 19990215
AB WO 200047745 A UPAB: 20000918
NOVELTY - Nucleotide fragment (I) of a long terminal repeat (LTR)-RU5 region comprising a nucleotide sequence which encodes the expression of an Multiple Sclerosis retrovirus (MSRV-1) protein (II) and a complementary nucleotide fragment, are new.

DETAILED DESCRIPTION - Nucleotide fragment of a LTR-RU5 region comprises a nucleotide sequence which encodes the expression of a protein (II). (II) comprises a peptide sequence from MSRV-1 retrovirus of (III), (IV) or (V) of 76, 64 and 140 amino acids (aa) respectively.

INDEPENDENT CLAIMS are also included for the following:

(1) a nucleic acid probe for the detection of MSRV-1 retrovirus which comprises 10-1000 monomers and specifically hybridizes with (I) in high stringency conditions;

(2) a primer for the amplification by polymerization of a nucleic acid retroviral sequence of MSRV-1 virus which comprises 10-30 monomers and hybridizes to (I) in high stringency conditions;

(3) a protein (II) encoded by (I);

(4) a polypeptide (VI) comprising at least 6 aa of (V);

(5) a polyclonal or monoclonal antibody directed against (II) or (VI);

(6) a process for detecting in a biological sample the presence of MSRV-1 retrovirus comprising contacting a probe of (1) with the biological sample and determining whether the probe binds to nucleic acid in the sample, where binding indicates the presence of MSRV-1 retrovirus;

(7) a process for detecting in a biological sample the presence of MSRV-1 retrovirus comprising contacting an antibody of (5) with the biological sample and determining whether the antibody binds to protein in the sample, where binding indicates the presence of MSRV-1 retrovirus; and

(8) a process for detecting in a biological sample the presence of MSRV-1 retrovirus comprising detecting the antigenic or biological properties of (II) or a fragment of (II).

USE - The probes and antibodies to MSRV-1 retrovirus protein are used to detect the presence of MSRV-1 retrovirus in a biological sample (claimed). The detection process can be used to identify and quantify, separate or isolate the substance or agent.

Dwg.0/3

L6 ANSWER 7 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2000-499229 [44] WPIDS
DNC C2000-149853
TI New nucleic acid from human endogenous retrovirus, useful e.g. for diagnosis of autoimmune disease and complications of pregnancy, contains at least part of the gag gene.
DC B04 D16
IN MALLET, F; **PARANHOS-BACCALA, G**; VOISSET, C
PA (INMR) BIO MERIEUX
CYC 22

PI WO 2000043521 A2 20000727 (200044)* FR 52
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
FR 2788784 A1 20000728 (200044)
EP 1147187 A2 20011024 (200171) FR
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002534980 W 20021022 (200301) 61
US 2004048298 A1 20040311 (200419)

ADT WO 2000043521 A2 WO 2000-FR144 20000121; FR 2788784 A1 FR 1999-888 19990121; EP 1147187 A2 EP 2000-900645 20000121, WO 2000-FR144 20000121; JP 2002534980 W JP 2000-594929 20000121, WO 2000-FR144 20000121; US 2004048298 A1 Cont of WO 2000-FR144 20000121, Cont of US 2001-869927 20010817, US 2003-632793 20030804

FDT EP 1147187 A2 Based on WO 2000043521; JP 2002534980 W Based on WO 2000043521

PRAI FR 1999-888 19990121

AB WO 200043521 A UPAB: 20000913
NOVELTY - Isolated, endogenous nucleic acid fragment (I), of retroviral type, comprises (or consists of) at least part of the gag gene of a retrovirus associated with either autoimmune disease, failure of pregnancy or disorders of pregnancy, and encodes, directly or indirectly, an expression product. Also included are complements of (I).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) isolated, endogenous transcription products (II) derived from at least part of the gag gene of (I);

(2) methods for detecting (I);

(3) method for studying and/or monitoring T cell proliferation in vitro by treating T cells with transcription/translation products of (I) or with derived or related synthetic peptides;

(4) process for in situ molecular labeling of isolated chromosomes using all or part of a specific (I) as probe;

(5) recombinant protein (P1) having a 363 amino acid sequence as defined in the specification; and

(6) reagent for detecting autoimmune disease or for monitoring pregnancy containing at least one (I) or derived proteins.

USE - (I), or proteins derived from it, are useful for diagnosis of autoimmune disease (specifically multiple sclerosis) and for monitoring pregnancy. (I) may also be used for in situ labeling of isolated chromosomes, while the transcription product from (I) can be used to study or monitor T cell proliferation in vitro.

Dwg.0/2

L6 ANSWER 8 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1999-394978 [33] WPIDS
CR 1996-190287 [20]
DNC C1999-116084
TI New Trypanosoma cruzi antigen.
DC B04 C06 D16
IN JOLIVET, M; LESENECHAL, M; MANDRAND, B; **PARANHOS-BACCALA, G**
PA (INMR) BIO MERIEUX
CYC 22
PI WO 9929867 A1 19990617 (199933)* EN
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: BR CA MX
EP 1045910 A1 20001025 (200055) EN
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
BR 9813489 A 20001017 (200056)
MX 2000005473 A1 20010401 (200171)

ADT WO 9929867 A1 WO 1998-IB1987 19981210; EP 1045910 A1 EP 1998-957050 19981210, WO 1998-IB1987 19981210; BR 9813489 A BR 1998-13489 19981210, WO 1998-IB1987 19981210; MX 2000005473 A1 MX 2000-5473 20000602
FDT EP 1045910 A1 Based on WO 9929867; BR 9813489 A Based on WO 9929867
PRAI US 1997-988242 19971210
AB WO 9929867 A UPAB: 20020711
NOVELTY - An antigenic determinant or epitope of the PTc40 protein from Trypanosoma cruzi comprising a fragment of 24 amino acids, from amino acids 403-426 of a fully defined 915 amino acid protein given in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a DNA or RNA sequence (I) comprising the sequence from nucleotides 1472-1543 of a fully defined 3402 bp cDNA sequence given in the specification, encoding the above PTc40n fragment;

(2) a putative promoter specific for Trypanosoma cruzi named SP6, for eukaryotic or prokaryotic expression of (I);

(3) expression cassette containing the putative promoter and DNA (I);

(4) a vector comprising the expression cassette;

(5) cell derived from a prokaryotic or eukaryotic organism, comprising the expression cassette integrated into the genome or the vector; and

(6) monoclonal or polyclonal antibodies obtained by immunological reaction of a human or animal organism with the PTc40 antigenic determinant.

ACTIVITY - None given.

MECHANISM OF ACTION - Vaccine. The antigenic relevance of G strain (GST)-Tc40 recombinant antigen was assessed by the immunoblot assay with a large panel of human serum samples from chronic chagasic patient (n = 201), non chagasic patients (leishmaniasis, toxoplasmosis, filariasis, leprosy, mononucleosis, rheumatoid arthritis, autoimmune diseases) (n = 67) and healthy individuals (n = 36). The Tc40 fusion protein reacted with 92% of the serum samples from chronic chagasic patients. Out of 103 non-chagasic sera tested, only one serum sample showed a reaction with the GST-Tc40 recombinant antigen. These results suggest that the presence of serum antibodies to the Tc40 antigen could be specifically associated with Chagas' disease.

USE - The PTc40 antigenic determinant is useful as a reagent for detection and/or monitoring of Trypanosoma cruzi infection from samples including blood serum or plasma, urine, saliva, or tears, by contacting with the sample and detecting an immune complex (claimed). The PTc40 antigenic determinant, the vector, expression cassette, cell or antibody are useful for treatment or prevention (vaccine) of a Trypanosoma cruzi infection in a man or animal (claimed).

ADVANTAGE - Current Trypanosoma cruzi antigens are obtained from protein fractions of the noninfectious stage of the parasite, and these do not allow sufficient production of antigens for use in reliable serological diagnostic tests. The strain to strain polymorphism reduces reliability of the tests.

Dwg.0/0

L6 ANSWER 9 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1998-322732 [28] WPIDS
CR 2003-512253 [48]; 2004-032461 [03]
DNN N1998-252312 DNC C1998-099357
TI New nucleic acid from retroviruses - useful for diagnosis, prevention and treatment of, e.g. multiple sclerosis.
DC B04 D16 S03
IN BEDIN, F; BESEME, F; JOLIVET-REYNAUD, C; KOMURIAN-PRADEL, F; MANDRAND, B;

PARANHOS-BACCALA, G; PERRON, H
PA (INMR) BIO MERIEUX
CYC 20
PI WO 9823755 A1 19980604 (199828)* EN 286
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP
EP 942987 A1 19990922 (199943) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2001505768 W 20010508 (200131) 279
ADT WO 9823755 A1 WO 1997-IB1482 19971126; EP 942987 A1 EP 1997-911411 19971126, WO 1997-IB1482 19971126; JP 2001505768 W WO 1997-IB1482 19971126, JP 1998-524475 19971126
FDT EP 942987 A1 Based on WO 9823755; JP 2001505768 W Based on WO 9823755
PRAI US 1996-756429 19961126
AB WO 9823755 A UPAB: 20040112
Isolated or purified nucleic acid (I) is: (a) a sequence of 2304 (S1) or 2364 (S2) bp respectively; (b) equivalents of S1 and S2, particularly sequences having for any 100 contiguous nt at least 50 (especially 80)% homology with (a), or (c) their complements, excluding HSERV-9 (human sequence of endogenous retrovirus-9) sequences. Also new are: (1) nucleic acid (Ia) encoding any polypeptide (II) having, for at least 30 contiguous aa, at least 50 (especially 70) % homology with a peptide encoded by S1, S2 or their complements; (2) nucleic acid (Ia) of retroviral type identical, or equivalent, to at least 1 part of the pol gene of isolated retrovirus associated with multiple sclerosis (MS) or rheumatoid arthritis (RA); (3) probes (II) that hybridise to (I); (4) primers derived from (I); (5) polypeptides (III) encoded by (I); (6) polypeptides (IV) that inhibit activity of (III), and (7) mono- or poly-clonal antibody (Ab) against MS associated retrovirus-1 (MSRV-1) raised against antigenic (III).
USE - (II), (III) and Ab are used to detect MSRV-1, or exposure to it, by usual immunoassay/hybridisation techniques.(I), (II) and Ab are used to diagnose infection by MS and RA-associated viruses, and also for prevention and treatment of infection with these viruses.
Dwg.0/53

L6 ANSWER 10 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1997-154266 [14] WPIDS
DNN N1997-127420 DNC C1997-049375
TI New viral material and nucleotide fragments associated with multiple sclerosis and rheumatoid arthritis - also related peptide(s) and antibodies, used for diagnosis, treatment and as vaccines.
DC B04 D16 S03
IN BEDIN, F; BESEME, F; JOLIVET-REYNAUD, C; KOMURIAN-PRADEL, F; MANDRAND, B; **PARANHOS-BACCALA, G**; PERRON, H; JOLIVET, R C; KOMURIAN, P F; PARANHOS, B G; PARANHOSBACCALA, G
PA (INMR) BIO MERIEUX
CYC 72
PI WO 9706260 A1 19970220 (199714)* FR 188
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
FR 2737500 A1 19970207 (199715) 107
AU 9668232 A 19970305 (199726)
NO 9701493 A 19970603 (199733)
EP 789077 A1 19970813 (199737) FR 121
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
BR 9606566 A 19971230 (199807)

CZ 9701357 A3 19980617 (199830)
SK 9700567 A3 19980909 (199848)
JP 11502416 W 19990302 (199919) 178
NZ 316080 A 19990429 (199923)
HU 9900425 A2 19990528 (199930)
US 6001987 A 19991214 (200005)
AU 730080 B 20010222 (200115)
US 6579526 B1 20030617 (200341)
US 2003186391 A1 20031002 (200365)

ADT WO 9706260 A1 WO 1996-FR1244 19960802; FR 2737500 A1 FR 1995-9643 19950803; AU 9668232 A AU 1996-68232 19960802; NO 9701493 A WO 1996-FR1244 19960802, NO 1997-1493 19970402; EP 789077 A1 EP 1996-420265 19960802; BR 9606566 A BR 1996-6566 19960802, WO 1996-FR1244 19960802; CZ 9701357 A3 WO 1996-FR1244 19960802, CZ 1997-1357 19960802; SK 9700567 A3 WO 1996-FR1244 19960802, SK 1997-567 19960802; JP 11502416 W WO 1996-FR1244 19960802, JP 1997-508179 19960802; NZ 316080 A NZ 1996-316080 19960802, WO 1996-FR1244 19960802; HU 9900425 A2 WO 1996-FR1244 19960802, HU 1999-425 19960802; US 6001987 A US 1996-691563 19960802; AU 730080 B AU 1996-68232 19960802; US 6579526 B1 Div ex US 1996-691563 19960802, US 1999-374766 19990816; US 2003186391 A1 Div ex US 1996-691563 19960802, Div ex US 1999-374766 19990816, US 2003-430442 20030507

FDT AU 9668232 A Based on WO 9706260; BR 9606566 A Based on WO 9706260; CZ 9701357 A3 Based on WO 9706260; JP 11502416 W Based on WO 9706260; NZ 316080 A Based on WO 9706260; HU 9900425 A2 Based on WO 9706260; AU 730080 B Previous Publ. AU 9668232, Based on WO 9706260; US 6579526 B1 Div ex US 6001987; US 2003186391 A1 Div ex US 6001987, Div ex US 6579526

PRAI FR 1995-9643 19950803

AB WO 9706260 A UPAB: 19970407

Isolated and purified viral material (A) includes, in the genome, (a) one of 10 sequences given in the specification (from about 400 bp to 2.5 kb); (b) their complements or (c) sequences equiv. to (a) and (b) and having at least 50, pref. 70, % homology with (a) and (b) over a stretch of 100 contiguous nucleotides. New nucleotide fragments (B) comprise: (i) any complete or partial genomic sequence of the pol gene of virus MSRV-1 (multiple sclerosis related virus), excluding a specified 1158 bp sequence (S1); (ii) all partial or complete genomic env or gag gene sequence of MSRV-1; (iii) any sequence that overlaps the pol and env or pol and gag genes; (iv) any partial or complete sequence from those 10 sequences from (A) given in the specification, i.e. from the clones FBd3, t pol, JLBc1, JLBc2, GM3, FBd13, LB19, LTRGAG12, FP6 and G+E+A, but excluding sequences identical to, or contg., S1; (v) sequences complementary to the above genomic sequences; (vi) any equiv. sequence; (B) does not comprise or include the ERV (endogenous retroviral)-9 sequence.

USE - All 10 of the sequences (A) are associated with MS; 6 are also associated with RA. (C) and Ab are useful for detection of MSRV-1 (or its specific antibodies), also for prevention and treatment, e.g. as a vaccine. (B) and related nucleic acid can be used similarly to detect infectious agents by hybridisation and to inhibit expression of these pathogens.

ADVANTAGE - MS and RA can now be detected at an early stage before symptoms are manifest.

Dwg.0/42

L6 ANSWER 11 OF 11 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1996-190287 [20] WPIDS
CR 1999-394978 [33]
DNN N1996-159056 DNC C1996-060808
TI New nucleic acid encoding Trypanosoma cruzi epimastigotic antigen - useful for diagnosis, monitoring and therapy of Chagas disease.

DC B04 D16 S03
IN JOLIVET, M; LESENECHAL, M; **PARANHOS-BACCALA, G**; PARANHOS, B G; MANDRAND, B
PA (INMR) BIO MERIEUX
CYC 65
PI FR 2723589 A1 19960216 (199620)* 5
    WO 9605312 A1 19960222 (199620)
       RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
        W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE
           KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE
           SG SI SK TJ TM TT UA UG US UZ VN
    AU 9531691 A 19960307 (199624)
    EP 723589   A1 19960731 (199635) FR
        R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
    BR 9506314 A 19970805 (199738)
    US 5820864 A 19981013 (199848)
    MX 9601346 A1 19980601 (200009)
    MX 194240   B 19991124 (200106)
    US 6270767 B1 20010807 (200147)
    US 6403103 B1 20020611 (200244)
    CA 2173957 C 20030325 (200324) FR
ADT FR 2723589 A1 FR 1994-10132 19940812; WO 9605312 A1 WO 1995-FR1071
    19950809; AU 9531691 A AU 1995-31691 19950809; EP 723589 A1 EP 1995-927775
    19950809, WO 1995-FR1071 19950809; BR 9506314 A BR 1995-6314 19950809, WO
    1995-FR1071 19950809; US 5820864 A US 1995-480917 19950607; MX 9601346 A1
    MX 1996-1346 19960410; MX 194240 B MX 1996-1346 19960410; US 6270767 B1
    Div ex US 1995-480917 19950607, US 1998-138736 19980824; US 6403103 B1 CIP
    of US 1995-480917 19950607, US 1997-988242 19971210; CA 2173957 C CA
    1995-2173957 19950809, WO 1995-FR1071 19950809
FDT AU 9531691 A Based on WO 9605312; EP 723589 A1 Based on WO 9605312; BR
    9506314 A Based on WO 9605312; US 6270767 B1 Div ex US 5820864; US 6403103
    B1 CIP of US 5820864; CA 2173957 C Based on WO 9605312
PRAI FR 1994-10132 19940812
AB FR 2723589 A UPAB: 20030410
    New DNA or RNA (I) contains at least one strand with a sequence identical, complementary (antisense) or homologous to a 3402 bp sequence (A) reproduced in the specification. Also new are: (1) protein (II) of apparent mol. wt. about 100 kD recognised by anti-Trypanosoma cruzi serum, also any immunological equiv. or fragment of (II), (2) expression cassette (EC) functional in a prokaryotic or eukaryotic organism able to express DNA encoding (II) or its fragments, (3) vectors contg. EC, (4) eukaryotic or prokaryotic cells contg. EC or such vector, (5) monoclonal or polyclonal antibodies (Ab) obtd. using (II) or its fragments as immunogen and (6) probes and primers that can hybridise to all or part of (A).

    USE - (I) encodes an antigen, designated PTc100t, present in the epimastigotic form of T. cruzi. Ab and (II) (partic. when immobilised on a support) are used to detect/monitor T. cruzi infection (Chagas disease, CD) by testing blood or other body fluids. The probes can also be used to identify T. cruzi. (II) can be used for active immunisation against CD, Ab for passive immunisation, while the probes can block transcription, translation and/or replication.

    ADVANTAGE - (II) can detect antibodies in all patients with CD.

    Dwg.1/2

=> e perron herve/in
E1   3   PERRON G M/IN
E2 24   PERRON H/IN
E3   0 --> PERRON HERVE/IN
E4 14   PERRON J/IN
E5   3   PERRON J C/IN

```
E6            1      PERRON J L/IN
E7            1      PERRON J M/IN
E8            1      PERRON J P/IN
E9            3      PERRON J S/IN
E10           1      PERRON K J/IN
E11          19      PERRON L/IN
E12          42      PERRON M/IN

=> s e2
L7           24 "PERRON H"/IN

=> s l7 not l6
L8           19 L7 NOT L6

=> d l8,bib,ab,1-19

L8   ANSWER 1 OF 19  WPIDS  COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN   2004-509287 [49]    WPIDS
DNN  N2004-402694        DNC C2004-188505
TI   Detection of pathological prion proteins, useful for diagnosis of
     spongiform encephalopathy, includes precipitation of the protein with an
     aminoglycoside antibiotic.
DC   B04 D16 S03
IN   BENCSIK, R A; COLEMAN, A W; MARTIN, A; MOUSSA, A; SHAHGALDIAN, P; PERRON,
     H
PA   (FRSE-N) AGENCE FR SECURITE SANITAIRES ALIMENTS; (CNRS) CNRS CENT NAT RECH
     SCI; (UYLY-N) UNIV LYON 1 BERNARD CLAUDE; (INMR) BIOMERIEUX SA
CYC  107
PI   FR 2849204       A1 20040625 (200449)*      24
     WO 2004059321    A1 20040715 (200449)  FR
        RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE
            LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP
            KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG
            PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ
            VC VN YU ZA ZM ZW
     AU 2003299389    A1 20040722 (200476)
ADT  FR 2849204 A1 FR 2002-16382 20021220; WO 2004059321 A1 WO 2003-FR3856
     20031219; AU 2003299389 A1 AU 2003-299389 20031219
FDT  AU 2003299389 A1 Based on WO 2004059321
PRAI FR 2002-16382         20021220
AB   FR   2849204 A UPAB: 20040802
     NOVELTY - Detecting or diagnosing the pathological prion protein (PrPsc)
     comprising treating a tissue or fluid sample, derived or obtained from a
     human or animal, with an antibiotic (I), preferably an aminoglycoside
     (Ia), is new.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
          (1) use of (Ia) for eliminating PrPsc from tissues or fluids; and
          (2) kit for diagnosing PrPsc-related diseases that contains (Ia).
          USE - The method is used for diagnosing PrPsc-associated diseases
     (e.g. scrapie in small ruminants, chronic wasting diseases of elk and
     antelope, BSE and CJD), particularly to prevent entry of affected animals
     into the human food chain. (Ia) are also used to eliminate PrPsc from
     tissues or fluids.
          ADVANTAGE - (Ia) concentrates PrPsc by precipitation, eliminating the
     need for ultracentrifugation.
     Dwg.0/6
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L8 ANSWER 2 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2004-501381 [48] WPIDS
DNN N2004-395892 DNC C2004-185869
TI Amplifying immunodetection of pathological prion protein, useful for diagnosis of spongiform encephalopathy, by adding a macrocyclic adjuvant ligand before reaction with antibody.
DC A26 A89 B04 D16 E19 S03
IN COLEMAN, A W; DA SILVA, E; MARTIN, A; MOUSSA, A; SHAHGALDIAN, P; DUPIN, M; LAZAR, A N; LECLERE, E; **PERRON, H**
PA (FRSE-N) AGENCE FR SECURITE SANITAIRES ALIMENTS; (CNRS) CNRS CENT NAT RECH SCI; (UYLY-N) UNIV LYON 1 BERNARD CLAUDE; (INMR) BIOMERIEUX SA
CYC 107
PI FR 2849205 A1 20040625 (200448)* 31
WO 2004059322 A1 20040715 (200448) FR
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
AU 2003299390 A1 20040722 (200476)
ADT FR 2849205 A1 FR 2002-16383 20021220; WO 2004059322 A1 WO 2003-FR3857 20031219; AU 2003299390 A1 AU 2003-299390 20031219
FDT AU 2003299390 A1 Based on WO 2004059322
PRAI FR 2002-16383 20021220
AB FR 2849205 A UPAB: 20040728
NOVELTY - Amplifying the immunodetection of pathological prion protein (PrPsc) comprising adding to the test sample a macrocyclic adjuvant ligand (MAL); treatment with protease K, then contacting the treated sample with anti-PrPsc antibodies (Ab).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for a kit for diagnosing PrPsc-related diseases, or for immunodetection of PrPsc, that contains MAL.

USE - The method is used for diagnosis of PrPsc-associated diseases (e.g. BSE, scrapie in small ruminants or CJD) or for immunodetection of PrPsc.

ADVANTAGE - The method allows detection of PrPsc at dilutions lower than possible with known methods, particularly it amplifies detection by at least a factor of 4.

Dwg.0/4

L8 ANSWER 3 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2004-102029 [11] WPIDS
DNC C2004-041906
TI Use of specific polypeptides of the calgranulin B family for diagnosis and therapy of degenerative, neurological or autoimmune diseases, especially multiple sclerosis.
DC B04 D16
IN CHARLES, M H; KOLBE, H; MALCUS, C; **PERRON, H**; ROECKLIN, D; SANTORO, L
PA (INMR) BIOMERIEUX STELHYS SNC
CYC 1
PI FR 2841786 A1 20040109 (200411)* 181
ADT FR 2841786 A1 FR 2003-7145 20030613
PRAI FR 2003-7145 20030613
AB FR 2841786 A UPAB: 20040213
NOVELTY - Use of at least one polypeptide (I), comprising at least part of a protein (II), to prepare a diagnostic, prognostic, prophylactic or

therapeutic composition for detection, prevention or treatment of a pathological state associated with degenerative, neurological and/or autoimmune diseases, is new.

DETAILED DESCRIPTION - Use of at least one polypeptide (I), comprising at least part of a protein (II), to prepare a diagnostic, prognostic, prophylactic or therapeutic composition for detection, prevention or treatment of a pathological state associated with degenerative, neurological and/or autoimmune diseases, is new. (II) comprises:

(a) any of SEQ IDs 17 (114 aa (amino acids)), 18 (93 aa); 19 (92 aa), 20 (92 aa), 21 (91 aa), 22 (93 aa) or 23 (92 aa), in native form;

(b) a sequence at least 70, preferably 98,% identical with (a); or

(c) a peptide sequence, or its fragment, belonging to the calgranulin B family.

INDEPENDENT CLAIMS are also included for:

(1) similar use of nucleic acid fragments (II) that encode (I);

(2) similar use of ligands (L) that are specific for (I) or (II);

(3) detecting either (I) or (L) by formation of a complex with the other of (I) and (L);

(4) detecting (I) by mass spectrometric analysis of a biological fluid; and

(5) use of (I) or (II) for testing the efficacy of therapeutic agents.

ACTIVITY - Neuroprotective; Nootropic; Antiparkinsonian; Antirheumatic; Antiarthritic; Dermatological; Immunosuppressive; Antiinflammatory.

No biological data given.

MECHANISM OF ACTION - Modulator of the activity or expression of a calgranulin B family member.

USE - (I), also the nucleic acid (II) that encodes it and ligands specific for (I) and (II) are used for detection, prevention or treatment of a pathological state associated with degenerative, neurological and/or autoimmune diseases, specifically multiple sclerosis but also Alzheimer's and Parkinson's diseases, amyotrophic lateral sclerosis, rheumatoid polyarthritis and lupus erythematosus, including use of immunogenic fragments of (I), or sequences encoding them, as vaccines, particularly in cases where the disease has been diagnosed at an early stage. (I) and (II) are also useful for testing efficacy of therapeutic agents.

Dwg.0/0

L8 ANSWER 4 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 2001-159475 [16] WPIDS
DNC C2001-047400
TI Detecting, preventing and treating degenerative, neurological and autoimmune diseases, particularly multiple sclerosis, using specified polypeptides or related nucleic acid or ligand.
DC B04 D16
IN CHARLES, M H; KOLBE, H; MALCUS, C; **PERRON, H**; ROECKLIN, D; SANTORO, L; CHARLES, M.
PA (INMR) BIOMERIEUX STELHYS SNC; (INMR) BIOMERIEUX STELHYS
CYC 95
PI WO 2001005422 A2 20010125 (200116)* FR 208
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
FR 2797402 A1 20010216 (200116)

AU 2000065768 A 20010205 (200128)
EP 1203239 A2 20020508 (200238) FR
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2003509340 W 20030311 (200319) 228
FR 2841787 A1 20040109 (200412)

ADT WO 2001005422 A2 WO 2000-FR2057 20000717; FR 2797402 A1 FR 1999-9372 19990715; AU 2000065768 A AU 2000-65768 20000717; EP 1203239 A2 EP 2000-953247 20000717, WO 2000-FR2057 20000717; JP 2003509340 W WO 2000-FR2057 20000717, JP 2001-510476 20000717; FR 2841787 A1 Div ex FR 1999-9372 19990715, FR 2003-7146 20030613

FDT AU 2000065768 A Based on WO 2001005422; EP 1203239 A2 Based on WO 2001005422; JP 2003509340 W Based on WO 2001005422

PRAI FR 1999-9372 19990715; FR 2003-7146 20030613

AB WO 200105422 A UPAB: 20010323

NOVELTY - Use of at least one polypeptide (A), containing at least fragment of a protein (B) selected from 28 sequences described in the specification, or having at least 70%, preferably 98% homology, to (B) or a fragment of one of the stated proteins, for detecting, preventing or treating a degenerative, neurological and/or auto-immune disease.

DETAILED DESCRIPTION - The sequences belong to the perlecan, precursor of the retinol-binding plasma protein, precursor of the ganglioside GM2 activator, calgranulin B or saposin B protein families.

INDEPENDENT CLAIMS are also included for the following:

(a) use of nucleic acids (C) that encode (A), or of the ligands (L) of (A) for detecting, preventing or treating a degenerative, neurological and/or autoimmune disease as for (A);

(b) use of (A) for preparation of immunogenic peptides;

(c) method for detecting (A), associated with a disease, by contacting (A) with (L) to form a complex of a complex or vice versa;

(d) polypeptide (A1) with a 193 amino acid sequence described in the specification, or fragments of it, provided these include at least one mutation relative to another 193 amino acid sequence (8) described in the specification;

(e) use of (A1) in the same ways as (A);

(f) nucleic acid (C1) encoding (A1);

(g) use of (C1) in the same ways as (C);

(h) method for detecting (A) and (A1) by mass spectrometry;

(i) diagnostic and prognostic method based on measuring at least one (A);

(j) use of (A), (C) or recombinant proteins encoded by (C), for testing the efficacy of therapeutic agents or for producing a pharmaceutical composition; and

(k) use of lycorin to produce a composition for preventing or treating a degenerative, neurological and/or autoimmune disease.

ACTIVITY - Antineurodegeneration; Immunomodulatory.

MECHANISM OF ACTION - Vaccine; Gene therapy.

USE - (A), also nucleic acid (C) encoding them and ligands of (A) and (C), are especially used for diagnosis, prognosis, prevention and treatment of multiple sclerosis (in its various forms and phases), but may also be useful in cases of e.g. Alzheimer's and Parkinson's diseases, amyotrophic lateral sclerosis, rheumatoid polyarthritis and lupus erythematosus, including use as vaccines and in gene therapy (expression of sense or antisense sequences). They can also be used to assess efficacy of potential therapeutic agents, particularly compounds that reduce or inhibit toxicity towards glial cells.

Dwg.0/18

L8 ANSWER 5 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text

AN 2000-638279 [61] WPIDS
DNN N2000-473425 DNC C2000-191994
TI Detecting superantigen activity, useful for identifying agents for treatment or prevention of autoimmune disease, from expansion or loss of particular lymphocyte Vbeta determinants.
DC B04 D16 S03
IN LAFONT, M; **PERRON, H**
PA (INMR) BIO MERIEUX
CYC 91
PI WO 2000057185 A1 20000928 (200061)* FR 133
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
FR 2791139 A1 20000922 (200061)
FR 2791140 A1 20000922 (200061)
AU 2000034377 A 20001009 (200103)
EP 1163522 A1 20011219 (200206) FR
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002539804 W 20021126 (200307) 123
ADT WO 2000057185 A1 WO 2000-FR691 20000320; FR 2791139 A1 FR 1999-3622 19990319; FR 2791140 A1 FR 1999-13755 19991028; AU 2000034377 A AU 2000-34377 20000320; EP 1163522 A1 EP 2000-912720 20000320, WO 2000-FR691 20000320; JP 2002539804 W JP 2000-607009 20000320, WO 2000-FR691 20000320
FDT AU 2000034377 A Based on WO 2000057185; EP 1163522 A1 Based on WO 2000057185; JP 2002539804 W Based on WO 2000057185
PRAI FR 1999-13755 19991028; FR 1999-3622 19990319
AB WO 200057185 A UPAB: 20001128
NOVELTY - A process for detecting activity of a superantigen (A) in a biological sample comprising identifying large scale expansion or loss of lymphocytes that carry at least 1 of the V beta 16 and/or V beta 17 determinants, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) method for detecting a pathological state (or predisposition to it) by detecting at least 1 of (A), stimulation of cytokine production (e.g. interleukin-6 or gamma -interferon), and induction of apoptosis;

(b) human retrovirus MRSV (not defined)-1, preferably endogenous, that has (A) activity, induced by expression of its env gene, or fragments of it that encodes at least 1 open reading frame of the env protein (542 amino acid sequence (P1) given in the specification)) and is associated with autoimmune disease;

(c) a nucleic acid (I) comprising at least 1 fragment of the RNA or DNA of the MRSV-1 env gene (1629 nucleotide (nt) sequence (N1) given in the specification), the fragment having at least 18, particularly 24, nt;

(d) a polypeptide (II) containing at least 1 fragment of (P1), containing at least 6, preferably 8, amino acids;

(e) a vector containing (I);

(f) methods for evaluating efficacy of an agent or composition for inhibition of (A) activity;

(g) a method for evaluating the prophylactic and/or therapeutic efficacy of an agent or composition with respect to a pathological condition (or predisposition) by application of method (f);

(h) a therapeutic and/or prophylactic composition containing an inhibitor of (A), optionally also excipient, adjuvant and/or diluent;

(i) a therapeutic and/or prophylactic composition containing an agent (B) that blocks interaction of (A) with antigen-presenting cells;

(j) a therapeutic and/or prophylactic composition containing a cell, preferably mammalian, genetically modified in vitro by a therapeutic agent that comprises at least 1 nucleic acid encoding inhibitors of (A) activity;

(k) a method for identifying substances (C) that block transcription and/or translation of MRSV-1; and

(l) a kit for screening substances for the ability to block the (A) activity of retroviruses, especially endogenous, associated with autoimmune disease.

ACTIVITY - Immunosuppressant.

MECHANISM OF ACTION - The envelope protein expressed by the endogenous human retrovirus MRSV-1 has superantigen activity associated with autoimmune disease.

USE - The method is used to screen for agents that inhibit (A), especially those associated with the endogenous human retrovirus MRSV-1 that is implicated in autoimmune disease, particularly multiple sclerosis. These agents are potentially useful for treatment or prevention (e.g. as vaccines) of autoimmune diseases.

Dwg.0/4

L8 ANSWER 6 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1999-156177 [14] WPIDS
DNC C1999-046189
TI Use of polypeptide derived from TRAIL protein for diagnosis of degenerative disease - autoimmunity and inflammation, also useful in prevention or treatment, and similar use of corresponding ligand and nucleic acid.
DC B04
IN BELLIVEAU, J F; **PERRON, H**; RIEGER, F
PA (INMR) BIO MERIEUX
CYC 21
PI FR 2766713 A1 19990205 (199914)* 21
WO 9907408 A1 19990218 (199914) FR
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
ADT FR 2766713 A1 FR 1997-10176 19970804; WO 9907408 A1 WO 1998-IB1195 19980804
PRAI FR 1997-10176 19970804
AB FR 2766713 A UPAB: 19990412
Use of a polypeptide (I) corresponding to at least the primary sequence of at least part of a protein (A) to produce a diagnostic, prophylactic or therapeutic composition useful in cases of degenerative, autoimmune and inflammatory diseases is new. (A), in its natural state, has a 281 amino acid (aa) sequence, reproduced, or is an equivalent of (1). Also new are similar uses for (i) ligand (L) specific for (I) and (ii) nucleic acid, RNA or DNA, encoding (I), or their equivalents or complements.

USE - The inventions can be used in treatment of neurodegenerative disease, lupus erythematosus, rhuematoid arthritis, and SEP. (I) is (a) apoptotic in central nervous sysytem cells; (b) antigenic and (c) recognises specifically the surface receptor of the TRAIL protein. (I) is a marker of disease and a therapeutic target, e.g. its apoptotic activity can be blocked with an anti-TRAIL antibody or a TRAIL equivalent that binds to specific receptors, inhibiting formation of natural complex. Also soluble TRAIL receptors can be targeted, with anti-receptor antibodies. (L) are used to detect proteins associated with the specified diseases, while (I) are used to detect antibodies associated with them. Specifically the disease is multiple sclerosis (MS) but may also be rheumatoid polyarthritis and lupus. Antisense fragments of nucleic acids encoding (I) and (L) may be used therapeutically.

Dwg.0/0

L8 ANSWER 7 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1999-120897 [10] WPIDS
DNN N1999-088147 DNC C1999-035496
TI New nucleic acid sequences from human endogenous retrovirus-W - expressed exclusively in placenta and useful in diagnosis and therapy of autoimmune disease, and abnormal or failed pregnancy.
DC B04 D16 S03
IN BESEME, F; BLOND, J; BOUTON, O; MALLET, F; MANDRAND, B; **PERRON, H**
PA (INMR) BIO MERIEUX
CYC 84
PI WO 9902696 A1 19990121 (199910)* FR 105
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9884470 A 19990208 (199924)
EP 1000158 A1 20000517 (200028) FR
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002512530 W 20020423 (200243) 97
US 2004176314 A1 20040909 (200459)
ADT WO 9902696 A1 WO 1998-FR1442 19980706; AU 9884470 A AU 1998-84470 19980706; EP 1000158 A1 EP 1998-935106 19980706, WO 1998-FR1442 19980706; JP 2002512530 W WO 1998-FR1442 19980706, JP 1999-508244 19980706; US 2004176314 A1 Cont of WO 1998-FR1442 19980706, Cont of US 1999-446024 19991216, US 2003-717580 20031121
FDT AU 9884470 A Based on WO 9902696; EP 1000158 A1 Based on WO 9902696; JP 2002512530 W Based on WO 9902696
PRAI FR 1997-8815 19970707
AB WO 9902696 A UPAB: 19990310
New retroviral genomic material (I), isolated, purified and at least partly functional, comprises (a) one of sequences (N1)-(N15), reproduced, of 1321, 2938, 1422, 2006, 1948, 1136, 2782, 666, 3372, 2372, 7582, 2563, 2585, 2575 and 783 bp,, respectively; (b) complements or equivalents of (a), particularly having, for any sequence of 100 contiguous nucleotides (nt) at least 70, particularly at least 90,% homology with (N1)-(N15), or encoding a polypeptide having, for any sequence of at least 30 amino acids (aa), at least 80, preferably 90,% homology with a sequence encoded by (N1)-(N15). Also new are (A) retroviral subgenomic nucleic acid (Ia) identical with sequence (N11) except for at least one deletion; (B) nucleic acid fragments (II) of at least 100 bases from any of (I), (Ia) or their fragments, complements or equivalents, particularly those having for any 100 nt segment at least 50, particularly 70,% homology; (C) detection probes and amplification primers that hybridise specifically to (I), (Ia) or (II); (D) RNA, DNA or particularly replication vectors containing (II); (E) peptides (III) encoded by an open reading frame (orf) of (II).

USE - (a) (I), (Ia), (II) and (III) are markers of autoimmune disease (e.g. multiple sclerosis, rheumatoid polyarthritis, disseminated lupus erythematosus, insulin-dependent diabetes and related pathologies) and of abnormal or unsuccessful pregnancy; (b) (I), (Ia) and (II) are chromosomal markers for susceptibility to these conditions, or proximity markers of genes associated with this susceptibility, particularly by identifying and/or quantifying any (II), RNA or DNA in a biological sample, also they are used therapeutically.

ADVANTAGE - No advantage given.

Dwg.0/6

L8 ANSWER 8 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1999-098275 [09] WPIDS
DNC C1999-029242
TI Nucleic acid sequences of retrovirus called MSRV-1 - associated with multiple sclerosis or rheumatoid polyarthritis.
DC B04 D16
IN BEDIN, F; KOMURIAN-PRADEL, F; MALLET, F; MANDRAND, B; OTT, C; PARAHNOS-BACCALA, G; **PERRON, H**; SODOYER, M
PA (INMR) BIO MERIEUX
CYC 84
PI FR 2765588 A1 19990108 (199909)* 82
WO 9902666 A2 19990121 (199910) FR
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9885450 A 19990208 (199924)
EP 996731 A2 20000503 (200026) FR
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002509437 W 20020326 (200236) 101
ADT FR 2765588 A1 FR 1997-8816 19970707; WO 9902666 A2 WO 1998-FR1460 19980707; AU 9885450 A AU 1998-85450 19980707; EP 996731 A2 EP 1998-936467 19980707, WO 1998-FR1460 19980707; JP 2002509437 W WO 1998-FR1460 19980707, JP 1999-508255 19980707
FDT AU 9885450 A Based on WO 9902666; EP 996731 A2 Based on WO 9902666; JP 2002509437 W Based on WO 9902666
PRAI FR 1997-8816 19970707
AB FR 2765588 A UPAB: 19990302
The following are claimed:

(1) isolated or purified nucleic acid material comprising a nucleotide sequence selected from (i) the 310 bp, 635 bp, 1481 bp, 1329 bp, 1511 bp, 764 bp, 800 bp sequences given in the specification; (ii) sequences complementary to the sequences of (i); and (iii) sequences equivalent to the sequences of (i) and (ii), especially sequences having at least 50%, preferably at least 70%, homology with the sequences of (i) or (ii) for any stretch of 100 contiguous monomers; (2) isolated or purified nucleic acid material encoding a polypeptide having at least 50%, preferably at least 70%, homology with a peptide sequence selected from the 103, 77, 493, 162, 398 and 378 amino acid sequences given in the specification for any contiguous stretch of at least 30 amino acids; (3) retroviral nucleic acid material in which the pol gene comprises a nucleotide sequence identical or equivalent to the 310 bp sequence and its complements; (4) retroviral nucleic acid material in which the 5' end of the pol gene starts at nucleotide 1419 of the 1511bp sequence; (5) retroviral nucleic acid material in which the pol gene encodes a polypeptide having at least 50%, preferably at least 70%, homology with the 103 amino acid sequence for any contiguous stretch of at least 30 amino acids; (6) retroviral nucleic acid material in which the 3' end of the gag gene ends at nucleotide 1418 of 1511bp sequence; (7) retroviral nucleic acid material in which the env gene comprises a nucleotide sequence identical or equivalent to a sequence selected from 1481bp sequence and its complement; (8) retroviral nucleic acid material in which the env gene comprises a nucleotide sequence that starts at nucleotide 1 of the 1481 bp sequence and ends at nucleotide 233 of the 635 bp sequence; (9) retroviral nucleic acid material in which the env gene encodes a polypeptide having at least 50%, preferably at least 70%,

homology with the 493 aa sequence for any contiguous stretch of at least 30 amino acids; (10) retroviral nucleic acid material in which the U3R region of the 3' LTR comprises a nucleotide sequence that ends at nucleotide 617 of the 635 bp sequence; (11) retroviral nucleic acid material in which the RU5 region of the 5' LTR comprises a nucleotide sequence that starts at nucleotide 755 of 1329 bp sequence and ends at nucleotide 337 of the 764 bp sequence or the 800 bp sequence; (12) retroviral nucleic acid material comprising a sequence that starts of nucleotide 755 of the 1329bp sequence and ends at nucleotide 617 of the 635bp sequence; (13) retroviral nucleic acid material as in (1)-(12) that is associated with at least one autoimmune disease such as multiple sclerosis or rheumatoid polyarthritis; (14) a nucleotide fragment comprising a nucleotide sequence as in (1); (15) a nucleotide fragment comprising a nucleotide sequence encoding a polypeptide as in (2); (16) a nucleic acid probe for detecting a retrovirus associated with multiple sclerosis and/or rheumatoid polyarthritis, capable of specifically hybridising to a fragment as in (14) or (15) belonging to the genome of the retrovirus; (17) a primer for amplifying RNA or DNA of a retrovirus associated with multiple sclerosis and/or rheumatoid polyarthritis, comprising a nucleotide sequence identical or equivalent to at least a portion of the nucleotide sequence of a fragment as in one of (8)-(11), especially a sequence having at least 50%, preferably at least 70%, homology with this portion for any stretch of 10 contiguous monomers; (18) RNA or DNA, especially a replication and/or cloning vector, comprising a genomic fragment of nucleic acid material as in one of (1)-(7) or a fragment as in (14) or (15); (19) a peptide encoded by any open reading frame belonging to a nucleotide fragment as in (14) or (15), especially a polypeptide, e.g. an oligopeptide, forming or comprising an antigenic determinant recognised by the sera of patients infected with the virus MSRV-1 and/or in whom the MSRV-1 virus has been reactivated.

USE - Also claimed are: (20) a diagnostic, prophylactic or therapeutic composition for inhibiting expression of at least one retrovirus associated with multiple sclerosis and/or rheumatoid polyarthritis, comprising a nucleotide fragment as in (14) or (15); (21) a method for detecting a retrovirus associated with multiple sclerosis and/or rheumatoid polyarthritis, comprising contacting RNA and/or DNA presumed to belong to or originate from the retrovirus, or the corresponding complementary RNA and/or DNA, with a composition comprising a nucleotide fragment as in (14) or (15).

Dwg.0/11

L8 ANSWER 9 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1998-586098 [50] WPIDS
CR 1998-586097 [50]
DNN N1998-456938 DNC C1998-175515
TI Peptides reactive with multiple sclerosis antibodies - useful for diagnosis or vaccine preparation.
DC B04 D16 S03
IN JOLIVET, R C; MANDRAND, B; **PERRON, H**; JOLIVET-REYNAUD, C.
PA (INMR) BIO MERIEUX
CYC 22
PI FR 2762601 A1 19981030 (199850)* 43
WO 9849285 A1 19981105 (199850) FR
RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
EP 975747 A1 20000202 (200011) FR
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002510967 W 20020409 (200227) 65
US 6555091 B1 20030429 (200331)

ADT FR 2762601 A1 FR 1997-16870 19971231; WO 9849285 A1 WO 1998-FR870 19980429; EP 975747 A1 EP 1998-922903 19980429, WO 1998-FR870 19980429; JP 2002510967 W JP 1998-546682 19980429, WO 1998-FR870 19980429; US 6555091 B1 WO 1998-FR870 19980429, US 1999-403343 19991018

FDT EP 975747 A1 Based on WO 9849285; JP 2002510967 W Based on WO 9849285; US 6555091 B1 Based on WO 9849285

PRAI FR 1997-5679 19970429

AB FR 2762601 A UPAB: 20030516

Peptides that specifically react with antibodies of multiple sclerosis (MS) patients and have the following amino acid sequences are new: (1) Gln Gln Ala Val; (2) Thr Gly Arg Pro; (3) Leu Gln Gln Ala Val Phe; (4) Ser Thr Gly Arg Pro Leu; (5) Arg Leu Val Leu Val Pro; (6) Phe Leu Glu Asn Gly Val; (7) Lys Gly Thr Ser Leu Ser; (8) Leu Ala Val Arg His Asp; (9) Thr Phe Asp Arg Arg Ile; (10) Asn Ala Cys Tyr Val Asp Leu Phe Leu Gly Ala Ser Val Cys Pro; (11) Ser Ser Ala Lys Ser His Cys Tyr Ala Phe Cys Ser Gly Leu Pro; (12) Met Pro Val Ser Arg Leu Cys Ile Glu Leu Asp Trp Cys Pro Pro; (13) Phe Cys Pro Pro Ile Leu Pro Tyr Ser Ala Trp Cys Pro Val Pro; (14) Glu Pro Met Thr Pro His Gln Trp Ile Thr Leu Tyr Arg Ser Tyr; (15) Asp Thr Pro Tyr Pro Trp Gly Trp Leu Leu Asp Glu Gly Tyr Asp; (16) Ser Arg Gly Ser His Glu Trp Ala Val Leu Phe Arg Phe Tyr Tyr; (17) Gln Ser Pro Leu Glu Asp Arg Ile Leu Arg Phe Leu Ser Pro Pro; (18) His Cys Arg Lys Val Thr Gly Ser Asp Tyr Leu Leu Cys Gly Leu; (19) Arg Gly Thr Gln Glu Trp Thr Glu Leu Trp Val Ser Phe Arg Ala. Also claimed are ''equivalents'' of the above peptides, including those based on the homology of peptide (11) to a foot-and-mouth disease SAT3 protein sequence and the homology of peptide (13) to a feline sarcoma virus (FSV) p30/p10/5'v-fsm sequence. Also claimed are polynucleotides encoding the peptides.

USE - The peptides can be used to diagnose or monitor MS. Peptides (1)-(4) can be used to detect the MS-associated retrovirus MSRV-1. The peptides can be used for ''fixation'' of MS or MSRV-1 antibodies in biological samples, especially serum, cerebrospinal fluid or urine. The peptides can be used to prepare vaccines.

Dwg.0/7

L8 ANSWER 10 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

Full Text

AN 1998-586097 [50] WPIDS

CR 1998-586093 [45]

DNN N1998-456937 DNC C1998-175514

TI Peptides reactive with multiple sclerosis antibodies - useful for diagnosis or vaccine preparation.

DC B04 D16 S03

IN JOLIVET, R C; MANDRAND, B; **PERRON, H**

PA (INMR) BIO MERIEUX

CYC 1

PI FR 2762600 A1 19981030 (199850)* 52

ADT FR 2762600 A1 FR 1997-5679 19970429

PRAI FR 1997-5679 19970429

AB FR 2762600 A UPAB: 19981217

Peptides that specifically react with antibodies of multiple sclerosis (MS) patients and have the following amino acid sequences are new: (1) Gln Gln Ala Val; (2) Thr Gly Arg Pro; (3) Leu Gln Gln Ala Val Phe; (4) Ser Thr Gly Arg Pro Leu; (5) Arg Leu Val Leu Val Pro; (6) Phe Leu Glu Asn Gly Val; (7) Lys Gly Thr Ser Leu Ser; (8) Leu Ala Val Arg His Asp; (9) Thr Phe Asp Arg Arg Ile; (10) Asn Ala Cys Tyr Val Asp Leu Phe Leu Gly Ala Ser Val Cys Pro; (11) Ser Ser Ala Lys Ser His Cys Tyr Ala Phe Cys Ser Gly Leu Pro; (12) Met Pro Val Ser Arg Leu Cys Ile Glu Leu Asp Trp Cys Pro Pro; (13) Phe Cys Pro Pro Ile Leu Pro Tyr Ser Ala Trp Cys Pro Val Pro; (14) Glu Pro Met Thr Pro His Gln Trp Ile Thr Leu Tyr Arg Ser Tyr; (15) Asp Thr Pro Tyr Pro Trp Gly Trp Leu Leu Asp Glu Gly Tyr Asp; (16) Ser Arg Gly Ser His Glu Trp

Ala Val Leu Phe Arg Phe Tyr Tyr; (17) Gln Ser Pro Leu Glu Asp Arg Ile Leu Arg Phe Leu Ser Pro Pro; (18) His Cys Arg Lys Val Thr Gly Ser Asp Tyr Leu Leu Cys Gly Leu. Also claimed are ''equivalents'' of the above peptides, including those based on the homology of peptide (11) to a foot-and-mouth disease SAT3-protein sequence and the homology of peptide (13) to a feline sarcoma virus (FSV) p30/p10/5'v-fsm sequence. Also claimed are polynucleotides encoding the peptides.

USE - The peptides can be used to diagnose or monitor MS. Peptides (1)-(4) can be used to detect the MS-associated retrovirus MSRV-1. The peptides can be used for ''fixation'' of MS or MSRV-1 antibodies in biological samples, especially serum, cerebrospinal fluid or urine. The peptides can be used to prepare vaccines.

Dwg.0/6

L8 ANSWER 11 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1998-446950 [38] WPIDS
DNN N1998-348398 DNC C1998-135559
TI Use of peptide derived from urinary protein of multiple sclerosis patients - for treatment, prevention and diagnosis of degenerative and auto immune diseases, also similar use of related ligands and nucleic acid.
DC B04 D16 S03
IN BACCALA, G; BISCHOFF, R; CHARLES, M; KOLBE, H; MALCUS-VOCANSON, C; MANDRAND, B; **PERRON, H**; ROECKLIN, D; CHARLES, M H; MALCUS, V C; MALCUSVOCANSON, C
PA (INMR) BIO MERIEUX
CYC 81
PI WO 9834637 A1 19980813 (199838)* FR 30
RW: AT BE CH DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
FR 2759371 A1 19980814 (199838)
AU 9866259 A 19980826 (199902)
ADT WO 9834637 A1 WO 1998-FR236 19980206; FR 2759371 A1 FR 1997-1772 19970207; AU 9866259 A AU 1998-66259 19980206
FDT AU 9866259 A Based on WO 9834637
PRAI FR 1997-1772 19970207
AB WO 9834637 A UPAB: 19981028
Use of a polypeptide (I) which comprises at least part of a protein (II) that, in native form, includes the sequence (A) (given in one letter amino acid code, see below) provided that (I) is not eosinophil cationic protein (ECP), for diagnosis, prevention and treatment of degenerative and/or autoimmune diseases. XPPQFTXAXXFXXQH (A) X = any amino acid, Also claimed are: (1) the use as above of two or more (I) in combination; (2) the use of a ligand (L) for (I) to obtain a diagnostic or therapeutic composition for diagnosis, prevention and treatment of degenerative and/or autoimmune diseases; and (3) the use of a nucleic acid fragment which encodes (A), its complement or their analogues with at least 70% homology to obtain a diagnostic or therapeutic composition for diagnosis, prevention and treatment of degenerative and/or autoimmune diseases.

USE - The methods are specifically applied to multiple sclerosis (MS) (but also rheumatoid polyarthritis and lupus erythematosus). Specifically (L) is used to detect proteins associated with these diseases and (I) are used to detect disease-related antibodies (both by complex formation), particularly in cerebrospinal fluid, serum or urine.

Dwg.0/0

L8 ANSWER 12 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1998-271671 [24] WPIDS
DNN N1998-213385 DNC C1998-084671
TI Detection and/or quantification of gliotoxic factor associated with sclerotic plaques - by incubating a fraction of urine sample with macroglial cells, e.g. immortalised astrocyte(s) and detecting and/or quantifying dead and/or living cells.
DC B04 D16 S03
IN MALCUS-VOCANSON, C; MANDRAND, B; **PERRON, H**; MALCUSVOCANSON, C
PA (INMR) BIO MERIEUX
CYC 21
PI WO 9811439 A1 19980319 (199824)* FR 38
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP US
EP 925504 A1 19990630 (199930) FR
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
EP 925504 B1 20010314 (200116) FR
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2001504686 W 20010410 (200128) 33
DE 69704279 E 20010419 (200129)
US 6270953 B1 20010807 (200147)
ES 2157569 T3 20010816 (200156)
ADT WO 9811439 A1 WO 1997-FR1620 19970912; EP 925504 A1 EP 1997-919095 19970912, WO 1997-FR1620 19970912; EP 925504 B1 EP 1997-919095 19970912, WO 1997-FR1620 19970912; JP 2001504686 W WO 1997-FR1620 19970912, JP 1998-513329 19970912; DE 69704279 E DE 1997-604279 19970912, EP 1997-919095 19970912, WO 1997-FR1620 19970912; US 6270953 B1 WO 1997-FR1620 19970912, US 1999-202118 19990329; ES 2157569 T3 EP 1997-919095 19970912
FDT EP 925504 A1 Based on WO 9811439; EP 925504 B1 Based on WO 9811439; JP 2001504686 W Based on WO 9811439; DE 69704279 E Based on EP 925504, Based on WO 9811439; US 6270953 B1 Based on WO 9811439; ES 2157569 T3 Based on EP 925504
PRAI FR 1996-11347 19960912
AB WO 9811439 A UPAB: 19980617
The following are claimed: (1) a method for detecting and/or quantifying a gliotoxic factor in a urine sample, comprising incubating a fraction of the sample, optionally pretreated to enrich the gliotoxic factor, with a culture of macroglial cells, e.g. immortalised astrocytes and detecting and/or quantifying dead and/or living cells; (2) a method for detecting and/or quantifying a cytotoxic factor in a biological sample, where the factor is cytotoxic to adherent target cells and induces death of these cells by apoptosis, comprising incubating a fraction of the sample, optionally pretreated to enrich the factor, with a culture of adherent target cells and detecting and/or quantifying dead cells by using flow cytometry to detect at least 1 characteristic associated directly or indirectly with the apoptotic adherent cells in all or part of the culture, and(3) use of a urine sample for detecting a gliotoxic factor associated with sclerotic plaques.

The factor is a gliotoxic factor and the cells are macroglial cells, especially immortalised astrocytes. Apoptotic cells are detected by releasing the cells; treating them with an agent that fixes the cells and permeabilises their cytoplasmic membranes, especially ethanol; extracting intracellular DNA fragments resulting from apoptosis; staining residual cellular DNA, preferably with propidium iodide, and detecting the ploidy of the cells by flow cytometry. Apoptotic cells are detected by inducing necrosis in a sample of living macroglial cells different from the test sample; releasing the cells; staining the DNA debris resulting from

necrosis; detecting necrotic cells by flow cytometry, adjusting the cytometer to exclude necrotic cells, and detecting dead cells in the test sample. The sample is a urine sample.

ADVANTAGE - Use of urine samples eliminates the need for samples obtained by invasive means, e.g. cerebrospinal fluid (cf. WO 9521859). Dwg.0/2

L8 ANSWER 13 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1997-479844 [44] WPIDS
DNN N1997-400283 DNC C1997-152329
TI Non-human mammal having pathological signs characteristic of multiple sclerosis - without being transgenic, produced by injection with gliotoxic factor, useful for evaluating therapeutic agents, also antibodies against gliotoxic factor.
DC B04 D16 P14
IN BENJELLOUN, N; **PERRON, H**; RIEGER, F
PA (INMR) BIO MERIEUX
CYC 77
PI WO 9733466 A1 19970918 (199744)* FR 60
RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN YU
FR 2745974 A1 19970919 (199745) 57
AU 9721658 A 19971001 (199805)
EP 825811 A1 19980304 (199813) FR
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 11512623 W 19991102 (200003) 52
ADT WO 9733466 A1 WO 1997-FR469 19970314; FR 2745974 A1 FR 1996-3417 19960314; AU 9721658 A AU 1997-21658 19970314; EP 825811 A1 EP 1997-914408 19970314, WO 1997-FR469 19970314; JP 11512623 W JP 1997-532343 19970314, WO 1997-FR469 19970314
FDT AU 9721658 A Based on WO 9733466; EP 825811 A1 Based on WO 9733466; JP 11512623 W Based on WO 9733466
PRAI FR 1996-3417 19960314
AB WO 9733466 A UPAB: 19971105
Non-human mammal, modified without affecting its genome, shows at least 2 of the following pathological signs:

(a) the blood-brain barrier is open or permeable to water-soluble blood components which are not specific for the cerebral parenchyma;

(b) astrocyte disorders characterised by dis-organisation of the physiological network, loss of astrocyte 'feet' around capillaries, and gliosis;

(c) activation of microglial cells;

(d) plaques of demyelinisation, particularly around the cerebral trunk and/or cerebellar white matter;

(e) lesions of glial cells and endothelial cells of the central nervous system.

Also claimed is a monoclonal antibody (MAb) directed against gliotoxic factor (GF) and/or molecules induced (or modified) by the effects of GF.

USE - The animals are used:

(i) to measure effects of therapeutic agents, particularly antiinflammatories or those intended for treatment of multiple sclerosis (MS), or

(ii) to determine if therapeutic agents or processes are safe to use when applied to the diseased brain.

They can also be used to study the neuropathology of MS.

MAb are used to detect GF, also possibly for treatment of GF-related diseases.

ADVANTAGE - The specified lesions are similar to those found in humans with MS.

Dwg.0/11

L8 ANSWER 14 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1996-403990 [41] WPIDS
DNN N1996-340304 DNC C1996-126936
TI Diagnosis, treatment and prevention of rheumatoid polyarthritis - using retroviral or other pathogenic or infectious material from the PLI-2 or LM7PC cell lines, or related nucleic acid.
DC B04 D16 S03
IN BEDIN, F; BESEME, F; MALLET, F; MANDRAND, B; **PERRON, H**
PA (INMR) BIO MERIEUX; (PERR-I) PERRON H
CYC 70
PI EP 731168 A1 19960911 (199641)* FR 68
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
FR 2731356 A1 19960913 (199643) 116
WO 9628552 A1 19960919 (199643) FR 125
RW: EA KE LS MW OA SD SZ UG
W: AL AM AT AU AZ BB BG BR BY CH CN CZ DE DK EE ES FI GB GE HU IS KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG UZ VN
CA 2171242 A 19960910 (199702) FR
AU 9650073 A 19961002 (199703)
NO 9604760 A 19961108 (199705)
JP 08322579 A 19961210 (199708) 165
CZ 9603287 A3 19970312 (199717)
BR 9605926 A 19970902 (199741)
NZ 303694 A 19971124 (199802)
CN 1153530 A 19970702 (200306)
ADT EP 731168 A1 EP 1996-420070 19960305; FR 2731356 A1 FR 1995-2960 19950309; WO 9628552 A1 WO 1996-FR360 19960307; CA 2171242 A CA 1996-2171242 19960307; AU 9650073 A AU 1996-50073 19960307; NO 9604760 A WO 1996-FR360 19960307, NO 1996-4760 19961108; JP 08322579 A JP 1996-91642 19960308; CZ 9603287 A3 CZ 1996-3287 19960307, WO 1996-FR360 19960307; BR 9605926 A BR 1996-5926 19960307, WO 1996-FR360 19960307; NZ 303694 A NZ 1996-303694 19960307, WO 1996-FR360 19960307; CN 1153530 A CN 1996-190173 19960307, WO 1996-FR360 19960307
FDT AU 9650073 A Based on WO 9628552; CZ 9603287 A3 Based on WO 9628552; BR 9605926 A Based on WO 9628552; NZ 303694 A Based on WO 9628552; CN 1153530 A Based on WO 9628552
PRAI FR 1995-2960 19950309
AB EP 731168 A UPAB: 19961011
Use of purified or isolated viral material (A), having reverse transcriptase activity and being a member of the endogenous retrovirus family, for diagnosis, prevention or treatment of infection by, or reactivation of, (A), associated with rheumatoid polyarthritis (RPA) is new. (A) is derived from one of the strains POL-2 (ECACC V92072202) or MS7PG (ECACC V93010816), or their variants having 1 antigen recognised by an antibody directed against the corresp. antigen of one of the specified strains. Also new are (1) similar use of (i) nucleotide fragments of (A), (ii) pathogenic and/or infectious agents (B) other than (A) but derived from the same viral strains and/or (iii) polypeptides encoded by the nucleotide fragments; (2) (A)-related nucleotide fragments of 126, 648 bp and 648 bp and (B)-related nucleotide fragments of 87 and 705 bp, also their complements and equivs., and their fragments for use as specific primers and probes for amplification/hybridisation with DNA and DNA of (A)

and (B), respectively.

ADVANTAGE - A pathogenic agent associated with rheumatoid polyarthritis has been identified. The isolation of nucleic acid from the pathogenic agent has made possible diagnosis, treatment and prevention of RPA.

Dwg.0/20

L8 ANSWER 15 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1996-364868 [37] WPIDS
DNN N1996-307599
TI Reflected wave interference reduction device esp. for wideband aerial - has absorbent layer which is positioned between radome and aerial with absorption factor increasing with radial position to vary effective diameter with frequency.
DC W02
IN BOULINGRE, C; **PERRON, H**; RANNOU, J
PA (CSFC) THOMSON CSF SA; (CSFC) THOMSON CSF
CYC 2
PI FR 2729791 A1 19960726 (199637)* 8
US 5724052 A 19980303 (199816) 6
ADT FR 2729791 A1 FR 1988-7905 19880614; US 5724052 A US 1989-364674 19890516
PRAI FR 1988-7905 19880614
AB FR 2729791 A UPAB: 19960918
The device includes a radiation absorbent layer (30) which is positioned between the aerial (10) and a radome (20), close to the aerial. This layer has an absorption factor which increases from the centre towards the outside.

The layer offers low absorption to low frequency radiation from the periphery, but high absorption of the high radiating frequencies reflected from the radome. This can be achieved using an absorption layer with a central hole or by using several layers with increasing diameter holes stacked so the effective thickness increases away from the centre.

USE/ADVANTAGE - E.g. optical and quasi-optical wavelengths Different effective diameter for different frequencies radiated from surface. Central part of layer can be non-absorbent.

Dwg.2/4

L8 ANSWER 16 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1995-283776 [37] WPIDS
DNN N1995-215943 DNC C1995-128080
TI Two pathogenic or infectious agents associated with multiple sclerosis - one being a retrovirus, useful for early diagnosis, prevention and treatment.
DC B04 D16 S03
IN BEDIN, F; BESEME, F; MALLET, F; MANDRAND, B; **PERRON, H**
PA (INMR) BIO MERIEUX
CYC 59
PI WO 9521256 A1 19950810 (199537)* FR 104
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KE KG KP KR KZ LK LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN
FR 2715936 A1 19950811 (199537) 33
FR 2715937 A1 19950811 (199537) 69
FR 2715938 A1 19950811 (199537) 32
FR 2715939 A1 19950811 (199537) 39
CA 2141907 A 19950805 (199543) FR
EP 674004 A1 19950927 (199543) FR 60

R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

AU 9517114 A 19950821 (199547)
FI 9504699 A 19951003 (199601)
NO 9503925 A 19951204 (199606)
FR 2727428 A1 19960531 (199629) 55
FR 2728585 A1 19960628 (199633) 65
JP 08511170 W 19961126 (199708) 100
NZ 279855 A 19980527 (199827)
US 5800980 A 19980901 (199842)
US 5871745 A 19990216 (199914)
US 5871996 A 19990216 (199914)
AU 704440 B 19990422 (199927)
US 5962217 A 19991005 (199948)
US 6184025 B1 20010206 (200109)
US 6342383 B1 20020129 (200210)
EP 674004 B1 20041222 (200501) FR

R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE

JP 3611856 B2 20050119 (200507) 40
DE 69533863 E 20050127 (200510)

ADT WO 9521256 A1 WO 1995-FR142 19950206; FR 2715936 A1 FR 1994-1529 19940204; FR 2715937 A1 FR 1994-1532 19940204; FR 2715938 A1 FR 1994-1530 19940204; FR 2715939 A1 FR 1994-1531 19940204; CA 2141907 A CA 1995-2141907 19950206; EP 674004 A1 EP 1995-420027 19950206; AU 9517114 A AU 1995-17114 19950206; FI 9504699 A WO 1995-FR142 19950206, FI 1995-4699 19951003; NO 9503925 A WO 1995-FR142 19950206, NO 1995-3925 19951003; FR 2727428 A1 FR 1994-14322 19941124; FR 2728585 A1 FR 1994-15810 19941223; JP 08511170 W JP 1995-520426 19950206, WO 1995-FR142 19950206; NZ 279855 A NZ 1995-279855 19950206, WO 1995-FR142 19950206; US 5800980 A Div ex US 1995-384137 19950206, US 1995-471724 19950606; US 5871745 A Div ex US 1995-384137 19950206, US 1995-471969 19950606; US 5871996 A US 1995-384137 19950206; AU 704440 B AU 1995-17114 19950206; US 5962217 A Div ex US 1995-384137 19950206, US 1995-470006 19950606; US 6184025 B1 Div ex US 1995-384137 19950206, Div ex US 1995-471969 19950606, US 1998-200990 19981130; US 6342383 B1 Div ex US 1995-384137 19950206, US 1998-133411 19980813; EP 674004 B1 EP 1995-420027 19950206; JP 3611856 B2 JP 1995-520426 19950206, WO 1995-FR142 19950206; DE 69533863 E DE 1995-633863 19950206, EP 1995-420027 19950206

FDT AU 9517114 A Based on WO 9521256; JP 08511170 W Based on WO 9521256; NZ 279855 A Based on WO 9521256; AU 704440 B Previous Publ. AU 9517114, Based on WO 9521256; US 5962217 A Div ex US 5871996; US 6184025 B1 Div ex US 5871745, Div ex US 5871996; US 6342383 B1 Div ex US 5871996; JP 3611856 B2 Previous Publ. JP 08511170, Based on WO 9521256; DE 69533863 E Based on EP 674004

PRAI FR 1994-15810 19941223; FR 1994-1529 19940204;
FR 1994-1530 19940204; FR 1994-1531 19940204;
FR 1994-1532 19940204; FR 1994-14322 19941124

AB WO 9521256 A UPAB: 19950921

Compsn. (A) comprises 2 pathogenic and/or infectious agents, isolated or purified, associated with multiple sclerosis i.e. (1) agent (Ia) that is a human virus with reverse transcriptase activity and of the endogenous retroviral family, or its variant and (2) agent (Ib) or its variant. (Ia) and (Ib) are derived from the same viral strain, i.e. POL-2 (ECACC V92072202) or MS7PG (ECACC V93010816), or their variants. Alternatively (Ia) and (Ib) are produced by the same cell line, i.e. PLI-2 (ECACC 92072201) or LM7PC (ECACC 93010817) or other similar infected cell cultures.

USE - Nucleic acid fragments contg. sequences (1)-(12) are used for detecting agents associated with multiple sclerosis, also for prophylaxis and treatment. Probes of (6) may be used to separate and identify these agents, opt. in conjunction with amplification primers. (III), and

antibodies specific for them, can also be used for diagnosis, prophylaxis and therapy.

ADVANTAGE - Detection of the infectious agent allows early diagnosis of disease, before neurological symptoms appear.

Dwg.0/17

L8 ANSWER 17 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1995-276614 [37] WPIDS
DNN N1995-211547 DNC C1995-125403
TI Gliotoxic factor from patients with multiple sclerosis - is cytotoxic for astrocytes; useful in diagnosis, treatment and prophylaxis.
DC B04 D16 S03
IN DOBRANSKY, T; MANDRAND, B; **PERRON, H**; RIEGER, F
PA (INMR) BIO MERIEUX
CYC 62
PI EP 667354 A1 19950816 (199537)* FR 44
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
FR 2716198 A1 19950818 (199538) 86
WO 9521859 A1 19950817 (199538) FR 93
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN
CA 2142557 A 19950816 (199545) FR
AU 9518152 A 19950829 (199548)
FI 9504876 A 19951013 (199601)
NO 9504081 A 19951213 (199608)
JP 08511808 W 19961210 (199710) 80
US 5728540 A 19980317 (199818) 38
NZ 281260 A 19980527 (199827)
JP 2803910 B2 19980924 (199843) 37
US 5876954 A 19990302 (199916)
AU 701972 B 19990211 (199918)
EP 667354 B1 20010919 (200155) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69522725 E 20011025 (200171)
CA 2142557 C 20011120 (200176) FR
ADT EP 667354 A1 EP 1995-420031 19950215; FR 2716198 A1 FR 1994-1946 19940215; WO 9521859 A1 WO 1995-FR178 19950215; CA 2142557 A CA 1995-2142557 19950215; AU 9518152 A AU 1995-18152 19950215; FI 9504876 A WO 1995-FR178 19950215, FI 1995-4876 19951013; NO 9504081 A WO 1995-FR178 19950215, NO 1995-4081 19951013; JP 08511808 W JP 1995-521024 19950215, WO 1995-FR178 19950215; US 5728540 A Div ex US 1995-389164 19950215, US 1995-468670 19950606; NZ 281260 A NZ 1995-281260 19950215, WO 1995-FR178 19950215; JP 2803910 B2 JP 1995-521024 19950215, WO 1995-FR178 19950215; US 5876954 A US 1995-389164 19950215; AU 701972 B AU 1995-18152 19950215; EP 667354 B1 EP 1995-420031 19950215; DE 69522725 E DE 1995-622725 19950215, EP 1995-420031 19950215; CA 2142557 C CA 1995-2142557 19950215
FDT AU 9518152 A Based on WO 9521859; JP 08511808 W Based on WO 9521859; NZ 281260 A Based on WO 9521859; JP 2803910 B2 Previous Publ. JP 08511808, Based on WO 9521859; AU 701972 B Previous Publ. AU 9518152, Based on WO 9521859; DE 69522725 E Based on EP 667354
PRAI FR 1994-1946 19940215
AB EP 667354 A UPAB: 19950921
New isolated or purified gliotoxic factor (A) is toxic against human and animal astrocytes, causing cytomorphological breakdown of their network of intermediate filaments (IF), and/or degradation of IF proteins and/or cell death, partic. by apoptosis.

USE - (A), natural, synthetic or recombinant, and ligands (esp.

antibodies), specific for it are useful in diagnosis, treatment and prophylaxis of multiple sclerosis (MS). Partic. detection and quantitation of (A) is used for diagnosis, monitoring and prognosis of the disease. Dwg.0/15

L8 ANSWER 18 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1993-336897 [42] WPIDS
CR 1993-336896 [42]
DNC C1993-149082
TI Viable cell culture infected with multiple sclerosis virus - prepd. by co-culturing prim. infected and permissive cells, then passaging, for virus identification and characterisation.
DC B04 D16
IN **PERRON, H**; SEIGNEURIN, J
PA (INMR) BIO MERIEUX; (UYGR-N) UNIV GRENOBLE FOURIER JOSEPH; (UYFO-N) UNIV FOURIER JOSEPH; (UYFO-N) UNIV FOURIER FOURIER
CYC 19
PI WO 9320189 A1 19931014 (199342)* FR 24
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA US
EP 592636 A1 19940420 (199416) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5585262 A 19961217 (199705) 6
EP 592636 B1 19981125 (199851) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69322227 E 19990107 (199907)
US 5925555 A 19990720 (199935)
CA 2110702 C 20040622 (200442) FR
ADT WO 9320189 A1 WO 1993-FR337 19930402; EP 592636 A1 EP 1993-908990 19930402, WO 1993-FR337 19930402; US 5585262 A WO 1993-FR337 19930402, US 1994-157060 19940202; EP 592636 B1 EP 1993-908990 19930402, WO 1993-FR337 19930402; DE 69322227 E DE 1993-622227 19930402, EP 1993-908990 19930402, WO 1993-FR337 19930402; US 5925555 A Div ex WO 1993-FR337 19930402, Div ex US 1994-157060 19940202, US 1996-651573 19960522; CA 2110702 C CA 1993-2110702 19930402, WO 1993-FR337 19930402
FDT EP 592636 A1 Based on WO 9320189; US 5585262 A Based on WO 9320189; EP 592636 B1 Based on WO 9320189; DE 69322227 E Based on EP 592636, Based on WO 9320189; US 5925555 A Div ex US 5585262; CA 2110702 C Based on WO 9320189
PRAI FR 1992-4322 19920403; FR 1992-13447 19921103
AB WO 9320189 A UPAB: 20040702
A viable, infected culture or cell line, comprising cells infected with at least one strain of the human virus associated with multiple sclerosis, is made by (1) growing human cells infected with the virus and, separately, non-infected permissive cells; (2) co-culturing samples of infected and permissive cells to give a first derived culture infected with virus; (3) cultivating the culture in series. Step (3) involves repeating the co-culture step using a new sample of permissive culture plus a sample of first derived culture (or its subculture) to give a new subculture which constitutes the viable viral culture.

Also new are (1) the infected cells (withdrawn from or belonging to the cultures prepd. as described), and derived cells in which the genome has been altered without changing the phenotype, and (2) a culture medium for use in the process.

Primary infected cells are pref. leptomeningeal cells; choroid plexus cells; nyeloid blood cells (esp. macrophages or monocytes) or lymphocytes, and permissive cells are esp. choroid plexus cells.

USE/ADVANTAGE - These cultures are partic. useful for identification and characterisation of the virus, but could also have clinical or

therapeutic application. They provide good replication and viral expression.
Dwg.0/2

L8 ANSWER 19 OF 19 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
Full Text
AN 1993-336896 [42] WPIDS
CR 1993-336897 [42]
DNN N1993-260345 DNC C1993-149081
TI Prodn. of cultures and cell lines contg. multiple sclerosis virus - by growing infected cells in medium contg. antibody against beta-interferon, also derived cells and viral material, useful e.g. in vaccines and diagnosis.
DC B04 D16 S03
IN **PERRON, H**; SEIGNEURIN, J; PERRON, A; RRON, H
PA (INMR) BIO MERIEUX; (UYGR-N) UNIV GRENOBLE FOURIER JOSEPH; (UYFO-N) UNIV FOURIER JOSEPH
CYC 19
PI WO 9320188 A1 19931014 (199342)* FR
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA US
FR 2689519 A1 19931008 (199348) 16
FR 2689520 A1 19931008 (199348) 38
FR 2689521 A1 19931008 (199348) 20
EP 587873 A1 19940323 (199412) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 592636 A1 19940420 (199416) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5585262 A 19961217 (199705) 6
US 5650318 A 19970722 (199735) 14
EP 957162 A1 19991117 (199953) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 587873 B1 20000119 (200009) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69327623 E 20000224 (200017)
ES 2142864 T3 20000501 (200028)
US 6071736 A 20000606 (200033)
US 6291225 B1 20010918 (200157)
CA 2110703 C 20011204 (200203) FR
ADT WO 9320188 A1 WO 1993-FR336 19930402; FR 2689519 A1 FR 1992-4322 19920403; FR 2689520 A1 FR 1992-13443 19921103; FR 2689521 A1 FR 1992-13447 19921103; EP 587873 A1 EP 1993-908989 19930402, WO 1993-FR336 19930402; EP 592636 A1 EP 1993-908990 19930402, WO 1993-FR337 19930402; US 5585262 A WO 1993-FR337 19930402, US 1994-157060 19940202; US 5650318 A WO 1993-FR336 19930402, US 1994-157061 19940202; EP 957162 A1 Div ex EP 1993-908989 19930402, EP 1999-113896 19930402; EP 587873 B1 EP 1993-908989 19930402, WO 1993-FR336 19930402, Related to EP 1999-113896 19930402; DE 69327623 E DE 1993-627623 19930402, EP 1993-908989 19930402, WO 1993-FR336 19930402; ES 2142864 T3 EP 1993-908989 19930402; US 6071736 A Cont of US 1994-157061 19940202, US 1996-754010 19961120; US 6291225 B1 Div ex WO 1993-FR336 19930402, Div ex US 1994-157061 19940202, US 1995-485145 19950607; CA 2110703 C CA 1993-2110703 19930402, WO 1993-FR336 19930402
FDT EP 587873 A1 Based on WO 9320188; EP 592636 A1 Based on WO 9320189; US 5585262 A Based on WO 9320189; US 5650318 A Based on WO 9320188; EP 957162 A1 Div ex EP 587873; EP 587873 B1 Related to EP 957162, Based on WO 9320188; DE 69327623 E Based on EP 587873, Based on WO 9320188; ES 2142864 T3 Based on EP 587873; US 6071736 A Cont of US 5650318; US 6291225 B1 Div ex US 5650318; CA 2110703 C Based on WO 9320188
PRAI FR 1992-13443 19921103; FR 1992-4322 19920403
AB WO 9320188 A UPAB: 20020114

A culture or cell line infected with a virus strain associated with multiple sclerosis (MS) is prepd. by (1) taking a body sample from an MS patient; (2) culturing this in medium favouring growth of infected cells to produce a culture of primary infected cells; (3) subjecting a sample of this (or of derived subculture) to successive passaging. The culture medium used contains an antibody (Ab) against beta-interferon (or an antigenically similar cpd.) which acts as an inhibitor of viral expression, to allow persistent expression of virus and propagation of the viral strain in the culture or cell line.

Also new are (1) prodn. of continuous cultures or cell lines infected with the viral; (2) culture media contg. Ab; (3) cell withdrawn from (or belonging to) cultures produced as above (also their derivs. in which the genome has been modified without affecting the phenotype); (4) method for transactivation of MS-related virus in such cells; (5) virus fractions isolated from these cells; and (6) immunological reactant comprising mono- or poly-clonal antibodies directed against antigenic viral extracts.

USE/ADVANTAGE - Antigenic extracts of the infected cells, or the new viral material (killed, inactivated or attenuated) are useful in vaccines and for detecting antibodies specific for MS-related virus.

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=> d his

     (FILE 'HOME' ENTERED AT 12:06:09 ON 04 APR 2005)

     FILE 'USPATFULL' ENTERED AT 12:06:16 ON 04 APR 2005
                E PARANHOS-BACCALA G/IN
L1           12 S E2
                E PERRON HERVE/IN
L2           22 S E3
L3           16 S L2 NOT L1
                E OTT CATHERINE/IN
                E MANDRAN BERNARD/IN
L4           47 S E5-E8
L5           30 S L4 NOT (L1 OR L2)

     FILE 'WPIDS' ENTERED AT 12:15:25 ON 04 APR 2005
                E PARANHOS BACCALA G/IN
L6           11 S E3
                E PERRON HERVE/IN
L7           24 S E2
L8           19 S L7 NOT L6

=> file medline
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              131.00     274.13

FILE 'MEDLINE' ENTERED AT 12:18:10 ON 04 APR 2005

 FILE LAST UPDATED: 2 APR 2005 (20050402/UP).  FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

 The MEDLINE reload for 2005 is now available.  For details enter HELP
 RLOAD at an arrow promt (=>).  See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
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OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> e paranhos baccala g/au
E1            4     PARANHOS AUGUSTO JR/AU
E2            3     PARANHOS BACALLA G S/AU
E3           18 --> PARANHOS BACCALA G/AU
E4            1     PARANHOS BACCALA G S/AU
E5            8     PARANHOS BACCALA GLAUCIA/AU
E6            1     PARANHOS DA COSTA M J/AU
E7            2     PARANHOS F/AU
E8            6     PARANHOS F R/AU
E9            2     PARANHOS G/AU
E10           1     PARANHOS G C/AU
E11           1     PARANHOS G D/AU
E12           1     PARANHOS G DA S/AU

=> s e2-e5
              3 "PARANHOS BACALLA G S"/AU
             18 "PARANHOS BACCALA G"/AU
              1 "PARANHOS BACCALA G S"/AU
              8 "PARANHOS BACCALA GLAUCIA"/AU
L9           30 ("PARANHOS BACALLA G S"/AU OR "PARANHOS BACCALA G"/AU OR "PARANH
                OS BACCALA G S"/AU OR "PARANHOS BACCALA GLAUCIA"/AU)

=> d l9,cbib,ab,1-30

L9   ANSWER 1 OF 30     MEDLINE on STN
2005069061.     PubMed ID: 15699429.   Mapping of B-cell epitopes in a
     Trypanosoma cruzi immunodominant antigen expressed in natural infections.
     Lesenechal Mylene; Becquart Laurence; Lacoux Xavier; Ladaviere Laurent;
     Baida Renata C P; Paranhos-Baccala Glaucia; da Silveira Jose Franco.
     (UMR 2714 CNRS-bioMerieux, IFR 128 BioScience Lyon-Gerland, CERVI-21,
     Lyon, France. ) Clinical and diagnostic laboratory immunology, (2005 Feb)
     12 (2) 329-33.  Journal code: 9421292. ISSN: 1071-412X. Pub. country:
     United States. Language: English.
AB   Tc40 is an immunodominant antigen present in natural Trypanosoma cruzi
     infections.  This immunogen was thoroughly mapped by using overlapping
     amino acid sequences identified by gene cloning and chemical peptide
     synthesis.  To map continuous epitopes of the Tc40 antigen, an epitope
     expression library was constructed and screened with sera from human
     chagasic patients.  A major, linear B-cell epitope spanning residues 403
     to 426 (PAKAAAPPAA) was identified in the central domain of Tc40.  A
     synthetic peptide spanning this region reacted strongly with 89.8% of the
     serum samples from T. cruzi-infected individuals.  This indicates that the
     main antigenic site is defined by the linear sequence of the peptide
     rather than a conformation-dependent structure.  The major B-cell epitope
     of Tc40 shares a high degree of sequence identity with T. cruzi ribosomal
     and RNA binding proteins, suggesting the existence of cross-reactivity
     among these molecules.

L9   ANSWER 2 OF 30     MEDLINE on STN
2004479490.     PubMed ID: 15382175.   Antigenic relevance of F protein in
     chronic hepatitis C virus infection. Komurian-Pradel Florence; Rajoharison
     Alain; Berland Jean-Luc; Khouri Valerie; Perret Magali; Van Roosmalen
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Mark; Pol Stanislas; Negro Francesco; **Paranhos-Baccala Glaucia**. (UMR2142 CNRS-bioMerieux, IFR 128 BioSciences Lyon-Gerland, Lyon, France.) Hepatology (Baltimore, Md.), (2004 Oct) 40 (4) 900-9. Journal code: 8302946. ISSN: 0270-9139. Pub. country: United States. Language: English.

AB The hepatitis C virus (HCV) F protein is a recently described, frameshift product of HCV core encoding sequence of genotype 1a. Its function and antigenic properties are unknown. Using enzyme-linked immunosorbent assay, we assessed the prevalence of anti-F antibodies in 154 patients chronically infected with HCV, 65 patients with other liver diseases, and 121 healthy controls. For this purpose, we expressed a highly purified HCV F recombinant protein from HCV genotype 1a in Escherichia coli. Because the F protein shares the 10 first amino acids with the core protein, the anti-HCV F response was also assessed by a F recombinant protein deleted of its 10 first amino acids [Delta(1-10)-F]. Ninety-six (62%) of the 154 HCV serum samples reacted with the complete F recombinant protein, whereas 39 (25%) showed a weaker anti-Delta(1-10)F reactivity and 150 (97%) had anti-core antibodies. No reactivity against F, Delta(1-10)F, or core was detected in any of the controls. To exclude a potential cross-reaction of anti-F antibodies with anti-core antibodies, a specific enzyme-linked immunosorbent assay was performed for anti-core antibodies. The specificity of anti-F antibodies was confirmed using an F synthetic peptide. The prevalence of anti-F antibodies did not correlate with HCV RNA serum level, genotype, or stage of liver disease. Sequence analysis from 8 anti-F-positive and 5 anti-F-negative serum samples did not reveal any particular difference potentially accounting for their respective anti-F responses. In conclusion, the F protein elicits specific antibodies in 62% of individuals chronically infected with HCV; such anti-F response does not seem to be affected by the F sequence heterogeneity.

L9 ANSWER 3 OF 30 MEDLINE on STN

2004459403. PubMed ID: 15367612. Memory T-cell-mediated immune responses specific to an alternative core protein in hepatitis C virus infection. Bain Christine; Parroche Peggy; Lavergne Jean Pierre; Duverger Blandine; Vieux Claude; Dubois Valerie; Komurian-Pradel Florence; Trepo Christian; Gebuhrer Lucette; **Paranhos-Baccala Glaucia**; Penin Francois; Inchauspe Genevieve. (FRE 2736 Ecole Normale Superieure, Lyon, France.) Journal of virology, (2004 Oct) 78 (19) 10460-9. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB In vitro studies have described the synthesis of an alternative reading frame form of the hepatitis C virus (HCV) core protein that was named F protein or ARFP (alternative reading frame protein) and includes a domain coded by the +1 open reading frame of the RNA core coding region. The expression of this protein in HCV-infected patients remains controversial. We have analyzed peripheral blood from 47 chronically or previously HCV-infected patients for the presence of T lymphocytes and antibodies specific to the ARFP. Anti-ARFP antibodies were detected in 41.6% of the patients infected with various HCV genotypes. Using a specific ARFP 99-amino-acid polypeptide as well as four ARFP predicted class I-restricted 9-mer peptides, we show that 20% of the patients display specific lymphocytes capable of producing gamma interferon, interleukin-10, or both cytokines. Patients harboring three different viral genotypes (1a, 1b, and 3) carried T lymphocytes reactive to genotype 1b-derived peptides. In longitudinal analysis of patients receiving therapy, both core and ARFP-specific T-cell- and B-cell-mediated responses were documented. The magnitude and kinetics of the HCV antigen-specific responses differed and were not linked with viremia or therapy outcome. These observations provide strong and new arguments in favor of the synthesis, during natural HCV infection, of an ARFP derived from the core sequence. Moreover, the present data provide the first demonstration of

the presence of T-cell-mediated immune responses directed to this novel HCV antigen.

L9 ANSWER 4 OF 30 MEDLINE on STN

2004457359. PubMed ID: 15364440. Comparative immunogenicity analysis of modified vaccinia Ankara vectors expressing native or modified forms of hepatitis C virus E1 and E2 glycoproteins. Abraham Jean-Daniel; Himoudi Nourredine; Kien Francois; Berland Jean-Luc; Codran Audrey; Bartosch Birke; Baumert Thomas; **Paranhos-Baccala Glaucia**; Schuster Catherine; Inchauspe Genevieve; Kieny Marie Paule. (INSERM U544-Institut de Virologie, 67000 Strasbourg, France.) Vaccine, (2004 Sep 28) 22 (29-30) 3917-28. Journal code: 8406899. ISSN: 0264-410X. Pub. country: Netherlands. Language: English.

AB We have evaluated in C57/Bl6 and HLA-A2.1 transgenic mice the immunogenicity of three MVA vectors expressing either native HCV E1E2 polyprotein, truncated and secreted E1 (E'1(311)) and E2 (E'2(661)) proteins, or a chimeric E1E2 heterodimer presented at the plasma membrane. Immunization induced mainly a Th1 response in HLA-A2.1 transgenic mice while a Th2-type response was detected in C57/Bl6 mice. Comparison of the three vectors shows an increase in the humoral response when antigens are secreted or membrane bound, and slightly in the cellular response when antigens are exposed on the cell surface.

L9 ANSWER 5 OF 30 MEDLINE on STN

2004398665. PubMed ID: 15302945. Expression of hepatitis C virus proteins in epithelial intestinal cells in vivo. Deforges Severine; Evlashev Alexey; Perret Magali; Sodoyer Mireille; Pouzol Stephane; Scoazec Jean-Yves; Bonnaud Bertrand; Diaz Olivier; **Paranhos-Baccala Glaucia**; Lotteau Vincent; Andre Patrice. (INSERM U503, IFR128 Biosciences Lyon Gerland, 21 avenue Tony Garnier, 69365 Lyon cedex 07, France.) Journal of general virology, (2004 Sep) 85 (Pt 9) 2515-23. Journal code: 0077340. ISSN: 0022-1317. Pub. country: England: United Kingdom. Language: English.

AB Previous work on hepatitis C virus (HCV) led to the discovery of a new form of virus particle associating virus and lipoprotein elements. These hybrid particles (LVP for lipo-viro-particles) are enriched in triglycerides and contain at least apolipoprotein B (apoB), HCV RNA and core protein. These findings suggest that LVP synthesis could occur in liver and intestine, the two main organs specialized in the production of apoB-containing lipoprotein. To identify the site of LVP production, the genetic diversity and phylogenetic relationship of HCV quasispecies from purified LVP, whole serum and liver biopsies from chronically infected patients were studied. HCV quasispecies from LVP and liver differed significantly, suggesting that LVP were not predominantly synthesized in the liver but might also originate in the intestine. The authors therefore searched for the presence of HCV in the small intestine. Paraffin-embedded intestinal biopsies from 10 chronically HCV-infected patients and from 12 HCV RNA-negative controls (10 anti-HCV antibody-negative and two anti-HCV antibody-positive patients) were tested for HCV protein expression. HCV NS3 and NS5A proteins were stained in small intestine epithelial cells in four of the 10 chronically infected patients, and not in controls. Cells expressing HCV proteins were apoB-producing enterocytes but not mucus-secreting cells. These data indicate that the small intestine can be infected by HCV, and identify this organ as a potential reservoir and replication site. This further emphasizes the interaction between lipoprotein metabolism and HCV, and offers new insights into hepatitis C infection and pathophysiology.

L9 ANSWER 6 OF 30 MEDLINE on STN

2004046475. PubMed ID: 14748062. Characterization of mimotopes mimicking an immunodominant conformational epitope on the hepatitis C virus NS3

helicase. Jolivet-Reynaud Colette; Adida Anne; Michel Sandrine; Deleage Gilbert; **Paranhos-Baccala Glaucia**; Gonin Virginie; Battail-Poirot Nicole; Lacoux Xavier; Rolland Dominique. (Unite Mixte de Recherche UMR 2142 bioMerieux/CNRS, CERVI, Lyon, France.. jolivet@cervi-lyon.inserm.fr) . Journal of medical virology, (2004 Mar) 72 (3) 385-95. Journal code: 7705876. ISSN: 0146-6615. Pub. country: United States. Language: English.

AB The hepatitis C virus (HCV) nonstructural 3 (NS3) protein is composed of an amino terminal protease and a carboxyl terminal RNA helicase. NS3 contains major antigenic epitopes. The antibody response to NS3 appears early in the course of infection and is focused on the helicase region. However, this response cannot be defined by short synthetic peptides indicating the recognition of conformation-dependent epitopes. In this study, we have screened a dodecapeptide library displayed on phage with anti-NS3 mouse monoclonal antibodies (mAbs) that compete with each other and human anti-HCV NS3 positive sera. Two peptides (mimotopes) were selected that appeared to mimic an immunodominant epitope since they were recognized specifically by the different anti-NS3 mAbs of the study and by human sera from HCV infected patients. Homology search between the two mimotopes and the NS3 sequence showed that one of the two peptides shared amino acid similarities with NS3 at residues 1396-1398 on a very accessible loop as visualized on the three-dimensional structure of the helicase domain whereas the other one had two amino acids similar to nearby residues 1376 and 1378. Reproduced as synthetic dodecapeptides, the two mimotopes were recognized specifically by 19 and 22, respectively, out of 49 sera from HCV infected patients. These mimotopes allowed also the detection of anti-NS3 antibodies in sera of HCV patients at the seroconversion stage. These results suggest that the two NS3 mimotopes are potential tools for the diagnosis of HCV infection.

L9 ANSWER 7 OF 30 MEDLINE on STN

2004019019. PubMed ID: 14715313. Strand specific quantitative real-time PCR to study replication of hepatitis C virus genome. Komurian-Pradel Florence; Perret Magali; Deiman Birgit; Sodoyer Mireille; Lotteau Vincent; **Paranhos-Baccala Glaucia**; Andre Patrice. (UMR2142 CNRS-bioMerieux, IFR128 Biosciences Lyon-Gerland, 21 Avenue, Tony Garnier, 69365, Lyon Cedex 07, France.. pradel@cervi-lyon.inserm.fr) . Journal of virological methods, (2004 Mar 1) 116 (1) 103-6. Journal code: 8005839. ISSN: 0166-0934. Pub. country: Netherlands. Language: English.

AB Qualitative detection of negative hepatitis C virus (HCV) RNA has been used widely to demonstrate HCV replication. However, relative quantitation of both positive and negative HCV RNA strands has never been reported for studying viral genome replication. A strand specific real-time PCR carried out in the highly conserved 5'-non-coding region of HCV genome and monitored either by the DNA binding dye SYBR Green I or by molecular beacons is described. Using these techniques, it was found that negative HCV RNA strand was a 100-1000 times less abundant than the positive strand in the liver of HCV infected patients.

L9 ANSWER 8 OF 30 MEDLINE on STN

2002738156. PubMed ID: 12450695. Vaccination with an adenoviral vector encoding hepatitis C virus (HCV) NS3 protein protects against infection with HCV-recombinant vaccinia virus. Arribillaga Laura; de Cerio Ascension Lopez Diaz; Sarobe Pablo; Casares Noelia; Gorraiz Marta; Vales Africa; Bruna-Romero Oscar; Borras-Cuesta Francisco; **Paranhos-Baccala Glaucia**; Prieto Jesus; Ruiz Juan; Lasarte Juan Jose. (Department of Internal Medicine, Centro de Investigaciones Medicas Aplicadas (CIMA), University of Navarra, Pamplona, Spain.. larribi@alumni.unav.es) . Vaccine, (2002 Dec 13) 21 (3-4) 202-10. Journal code: 8406899. ISSN: 0264-410X. Pub. country: Netherlands. Language: English.

AB Cellular immune response plays an important role in the clearance of hepatitis C virus (HCV). Thus, development of efficient ways to induce anti-viral cellular immune responses is an important step toward prevention and/or treatment of HCV infection. With this aim, we have constructed a replication-deficient recombinant adenovirus expressing HCV NS3 protein (RAdNS3). The efficacy of RAdNS3 was tested in vivo by measuring the protection against infection with a recombinant vaccinia virus expressing HCV-polyprotein (vHCV1-3011). Immunisation with 10(9)pfu of RAdNS3 induced anti-NS3 humoral, T helper and T cytotoxic responses. We identified eight epitopes recognised by IFN-gamma producing cells, five of them exhibiting lytic activity. Moreover, we show that RAdNS3 immunised mice were protected against challenge with vHCV1-3011 and that this protection was mediated by CD8(+) cells. In conclusion, our results suggest that adenoviral vectors encoding NS3 might be useful for the induction of prophylactic and/or therapeutic anti-HCV immunity.

L9 ANSWER 9 OF 30 MEDLINE on STN

2002329869. PubMed ID: 12072493. Characterization of low- and very-low-density hepatitis C virus RNA-containing particles. Andre P; Komurian-Pradel F; Deforges S; Perret M; Berland J L; Sodoyer M; Pol S; Brechot C; **Paranhos-Baccala G**; Lotteau V. (INSERM U503, CERVI, Lyon, France.. andre@cervi-lyon.inserm.fr) . Journal of virology, (2002 Jul) 76 (14) 6919-28. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The presence of hepatitis C virus (HCV) RNA-containing particles in the low-density fractions of plasma has been associated with high infectivity. However, the nature of circulating HCV particles and their association with immunoglobulins or lipoproteins as well as the characterization of cell entry have all been subject to conflicting reports. For a better analysis of HCV RNA-containing particles, we quantified HCV RNA in the low-density fractions of plasma corresponding to the very-low-density lipoprotein (VLDL), intermediate-density lipoprotein, and low-density lipoprotein (LDL) fractions from untreated chronically HCV-infected patients. HCV RNA was always found in at least one of these fractions and represented 8 to 95% of the total plasma HCV RNA. Surprisingly, immunoglobulins G and M were also found in the low-density fractions and could be used to purify the HCV RNA-containing particles (lipo-viro-particles [LVP]). Purified LVP were rich in triglycerides; contained at least apolipoprotein B, HCV RNA, and core protein; and appeared as large spherical particles with a diameter of more than 100 nm and with internal structures. Delipidation of these particles resulted in capsid-like structures recognized by anti-HCV core protein antibody. Purified LVP efficiently bind and enter hepatocyte cell lines, while serum or whole-density fractions do not. Binding of these particles was competed out by VLDL and LDL from noninfected donors and was blocked by anti-apolipoprotein B and E antibodies, whereas upregulation of the LDL receptor increased their internalization. These results suggest that the infectivity of LVP is mediated by endogenous proteins rather than by viral components providing a mechanism of escape from the humoral immune response.

L9 ANSWER 10 OF 30 MEDLINE on STN

2002110763. PubMed ID: 11807230. Hepatitis C virus non-structural protein 3-specific cellular immune responses following single or combined immunization with DNA or recombinant Semliki Forest virus particles. Brinster C; Chen M; Boucreux D; **Paranhos-Baccala G**; Liljestrom P; Lemmonier F; Inchauspe G. (Unite Mixte CNRS/BioMerieux UMR 2142, Ecole Normale Superieure, 46 Allee d'Italie, 69364 Lyon Cedex 07, France.) Journal of general virology, (2002 Feb) 83 (Pt 2) 369-81. Journal code: 0077340. ISSN: 0022-1317. Pub. country: England: United Kingdom. Language:

English.

AB The capacity of recombinant Semliki Forest virus particles (rSFV) expressing the hepatitis C virus non-structural protein 3 (NS3) to induce, in comparison or in combination with an NS3-expressing plasmid, specific cellular and humoral immune responses in murine models was evaluated. In vitro studies indicated that both types of vaccine expressed the expected size protein, albeit with different efficacies. The use of mice transgenic for the human HLA-A2.1 molecule indicated that the rSFV-expressed NS3 protein induces, as shown previously for an NS3 DNA vaccine, NS3-specific cytotoxic lymphocytes (CTLs) targeted at one dominant HLA-A2 epitope described in infected patients. All DNA/rSFV vaccine combinations evaluated induced specific CTLs, which were detectable for up to 31 weeks after the first injection. Overall, less than 1 log difference was observed in terms of the vigour of the bulk CTL response induced and the CTL precursor frequency between all vaccines (ranging from 1:2.6x10(5) to 1:1x10(6)). Anti-NS3 antibodies could only be detected following a combined vaccine regimen in non-transgenic BALB/c mice. In conclusion, rSFV particles expressing NS3 are capable of inducing NS3-specific cellular immune responses targeted at a major HLA-A2 epitope. Such responses were comparable to those obtained with a DNA-based NS3 vaccine, whether in the context of single or combined regimens.

L9 ANSWER 11 OF 30 MEDLINE on STN

2001396207. PubMed ID: 11337053. Specific detection of RT activity in culture supernantants of retrovirus-producing cells, using synthetic DNA as competitor in polymerase enhanced reverse transcriptase assay. Voisset C; Tonjes R R; Breyton P; Mandrand B; **Paranhos-Baccala G.** (Unite Mixte de Recherche 2142 CNRS-bioMerieux, Ecole Normale Superieure de Lyon, 46, allee d'Italie, 69364 Cedex 07, Lyon, France.) Journal of virological methods, (2001 May) 94 (1-2) 187-93. Journal code: 8005839. ISSN: 0166-0934. Pub. country: Netherlands. Language: English.

AB The polymerase enhanced reverse transcriptase (PERT) assay is a highly sensitive assay for the detection of reverse transcriptase (RT) activity in culture supernatants of retrovirus-producing cells. However, some cellular DNA-dependent DNA polymerases exhibit RT-like activities in this assay. A synthetic DNA competitor which suppresses the RT-like activities of cellular DNA-dependent DNA polymerases was used in a modified PERT assay technique for specific detection of RT activity in culture supernatants of retrovirus-producing cells. We determined the optimum condition of the assay and evaluated its specificity. This improved PERT assay is easy to perform and is able to detect minute amounts of purified RT, as well as RT in crude cell lysates and concentrated culture supernatants.

L9 ANSWER 12 OF 30 MEDLINE on STN

2001297801. PubMed ID: 11377718. Quantitation of HCV RNA using real-time PCR and fluorimetry. Komurian-Pradel F; **Paranhos-Baccala G;** Sodoyer M; Chevallier P; Mandrand B; Lotteau V; Andre P. (UMR2142 CNRS-bioMerieux, 21 rue Tony Garnier, 69007, Lyon, France.) Journal of virological methods, (2001 Jun) 95 (1-2) 111-9. Journal code: 8005839. ISSN: 0166-0934. Pub. country: Netherlands. Language: English.

AB Real-time PCR technology may provide an accurate and sensitive method to quantify hepatitis C virus (HCV) RNA. So far, studies have been carried out using the Taqman technology with the ABI Prism 7700 sequence detector. An alternative and simple real-time PCR assay is described with no probe requirement, based on the SYBR Green I dye and LightCycler fluorimeter. Amplicon synthesis was monitored continuously by SYBR Green I dye binding to double stranded DNA during PCR of the 5' HCV non-coding (NC) region. Specificity was verified by amplicon melting temperatures. An external

standard curve was constructed with serial 10 fold dilutions of a modified synthetic HCV 5' NC RNA. A wide range linear relationship (up to 3.7x10(9) copies/ml) was observed between number of PCR cycle needed to detect a fluorescent signal and number of RNA copy. Intra- and inter-assay coefficients of variation were 0.7 to 2.1 and 3.7% respectively, indicating good reproducibility of the method. Thirty-three HCV positive sera of different genotypes were quantified by this method and gave similar but more sensitive results compared to the branched DNA (bDNA) technology.

L9 ANSWER 13 OF 30 MEDLINE on STN

2001095357. PubMed ID: 10948422. RNA amplification technique, NASBA, also amplifies homologous plasmid DNA in non-denaturing conditions. Voisset C; Mandrand B; **Paranhos-Baccala G.** (UMR103 CNRS-bioMerieux Ecole Normale Superieure de Lyon, France.) BioTechniques, (2000 Aug) 29 (2) 236-8, 240. Journal code: 8306785. ISSN: 0736-6205. Pub. country: United States. Language: English.

L9 ANSWER 14 OF 30 MEDLINE on STN

2000447323. PubMed ID: 10998223. Evaluation of an enzyme immunoassay for hepatitis C virus antibody detection using a recombinant protein derived from the core region of hepatitis C virus genome. Lopes E P; Granato C H; Lanzoni V; Granero L; **Paranhos-Baccala G;** Tomiyama H; Silva A E; Ferraz M L. (Escola Paulista de Medicina, Universidade Federal de Sao Paulo, Sao Paulo, SP, 04023-900, Brasil.) Memorias do Instituto Oswaldo Cruz, (2000 Sep-Oct) 95 (5) 717-20. Journal code: 7502619. ISSN: 0074-0276. Pub. country: Brazil. Language: English.

AB This study was undertaken to evaluate an enzyme immunoassay (EIA) for hepatitis C virus antibody detection (anti-HCV), using just one antigen. Anti-HCV EIA was designed to detect anti-HCV IgG using on the solid-phase a recombinant C22 antigen localized at the N-terminal end of the core region of HCV genome, produced by BioMerieux. The serum samples diluted in phosphate buffer saline were added to wells coated with the C22, and incubated. After washings, the wells were loaded with conjugated anti-IgG, and read in a microtiter plate reader (492 nm). Serum samples of 145 patients were divided in two groups: a control group of 39 patients with non-C hepatitis (10 acute hepatitis A, 10 acute hepatitis B, 9 chronic hepatitis B, and 10 autoimmune hepatitis) and a study group consisting of 106 patients with chronic HCV hepatitis. In the study group all patients had anti-HCV detected by a commercially available EIA (Abbott), specific for HCV structural and nonstructural polypeptides, alanine aminotransferase elevation or positive serum HCV-RNA detected by nested-PCR. They also had a liver biopsy compatible with chronic hepatitis. The test was positive in 101 of the 106 (95%) sera from patients in the study group and negative in 38 of the 39 (97%) sera from those in the control group, showing an accuracy of 96%. According to these results, our EIA could be used to detect anti-HCV in the serum of patients infected with hepatitis C virus.

L9 ANSWER 15 OF 30 MEDLINE on STN

2000417349. PubMed ID: 10826480. Chromosomal distribution and coding capacity of the human endogenous retrovirus HERV-W family. Voisset C; Bouton O; Bedin F; Duret L; Mandrand B; Mallet F; **Paranhos-Baccala G.** (Unite Mixte 103 CNRS-bioMerieux, Ecole Normale Superieure de Lyon, France.) AIDS research and human retroviruses, (2000 May 20) 16 (8) 731-40. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB Some genomic elements of the multicopy HERV-W endogenous retroviral family have been previously identified in databases. One of them, located on chromosome 7, contains a single complete open reading frame (ORF)

putatively encoding an envelope protein. We have experimentally investigated the genomic complexity and coding capacity of the HERV-W family. The human haploid genome contains at least 70, 100, and 30 HERV-W-related gag, pro, and env regions, respectively, widely and heterogeneously dispersed among chromosomes. Using in vitro transcription-translation procedures, three putative HERV-W gag, pro, and env ORFs were detected on chromosomes 3, 6, and 7, respectively, and their sequences analyzed. A 363 amino acid gag ORF containing matrix and carboxy-terminal truncated capsid domains encoded a putative 45-kDa protein. No gag-pro ORF was found, but a pro sequence containing a DTG active site was detected. Finally, the previously described 538 amino acid HERV-W env ORF, located on chromosome 7, was shown to be unique and encoded a putative 80-kDa glycosylated protein. Proteins of molecular mass identical to the one obtained by an in vitro transcription-translation procedure were detected in human placenta, using anti HERV-W Gag- and Env-specific antibodies. The absence of an HERV-W replication-competent provirus versus the existence of HERV-W-related Gag and Env proteins in healthy human placenta is discussed with respect to particle formation, physiology, and pathology.

L9 ANSWER 16 OF 30 MEDLINE on STN

2000112908. PubMed ID: 10644845. Identification of a human epitope in hepatitis C virus (HCV) core protein using a molecularly cloned antibody repertoire from a non-symptomatic, anti-HCV-positive patient. Barban V; Fraysse-Corgier S; **Paranhos-Baccala G**; Petit M; Manin C; Berard Y; Prince A M; Mandrand B; Meulien P. (Research Department, Pasteur Merieux Connaught, 69290 Marcy l'Etoile, France.. vbarban@fr.pmc-vacc.com) . Journal of general virology, (2000 Feb) 81 (Pt 2) 461-9. Journal code: 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Healthy carriers of hepatitis C virus (HCV) infection exhibit a specific antibody response against all HCV antigens, which could play a role in disease control. Generation of panels of human antibodies may permit a thorough characterization of this response and further identify particular antibodies with potential clinical value. To this effect, we have established a human phage-display antibody library from a patient exhibiting a high antibody response against HCV antigens and no clinical symptoms of disease. This library was screened against a recombinant core antigen [amino acids (aa) 1-119] produced in E. coli. Two recombinant Fab-carrying phages (rFabCs) were isolated and characterized. Both rFabC3 and rFabC14 recognize aa 1-48 on core antigen, but rFabC14 is competed out by a synthetic peptide, C(2-20) (aa 1-20), at much lower concentrations than rFabC3. In order to identify more precisely the recognition sites of these antibodies, we produced soluble forms of the rFabs (sFabs), and used them to pan a random phage-display peptide library. A single peptide sequence, QLITKPL, was identified with sFabC3, while two equally represented sequences, HAFPHLH and SAPSSKN, were isolated using sFabC14. The QLITKPL sequence was partially localized between aa 8 and 14 of core protein, but no clear homology was found for the two sFabC14 peptides. However, we confirmed the specificity of these peptides by competition experiments with sFabC14.

L9 ANSWER 17 OF 30 MEDLINE on STN

2000046348. PubMed ID: 10580403. Phylogeny of a novel family of human endogenous retrovirus sequences, HERV-W, in humans and other primates. Voisset C; Blancher A; Perron H; Mandrand B; Mallet F; **Paranhos-Baccala G**. (Unite Mixte de Recherche 103 CNRS-bioMerieux, Ecole Normale Superieure de Lyon, France.) AIDS research and human retroviruses, (1999 Nov 20) 15 (17) 1529-33. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB A novel human endogenous retrovirus, HERV-W, has been characterized on the basis of multiple sclerosis-associated retrovirus (MSRV) probes. We have analyzed the phylogenetic distribution of HERV-W in humans and other primate species. As HERV-W presents a C/D chimeric nature and is largely composed of deleted elements, Southern blots were performed using gag, pol, env, and LTR probes. The relative complexities observed for gag, pol, env, and LTR regions were similar in humans, apes, and Old World monkeys, the minimal number of bands observed after Southern blot analysis being 25, 50, 10, and at least 100, respectively. The HERV-W family entered the genome of catarrhines more than 25 million years ago.

L9 ANSWER 18 OF 30 MEDLINE on STN

2000034024. PubMed ID: 10568029. Heterologous expression of a Trypanosoma cruzi surface glycoprotein (gp82) in mammalian cells indicates the existence of different signal sequence requirements and processing. Ramirez M I; Boscardin S B; Han S W; **Paranhos-Baccala G**; Yoshida N; Kelly J M; Mortara R A; Da Silveira J F. (Departamento de Microbiologia, Imunologia e Parasitologia, Universidade Federal de Sao Paulo, Escola Paulista de Medicina, Brazil.) Journal of eukaryotic microbiology, (1999 Nov-Dec) 46 (6) 557-65. Journal code: 9306405. ISSN: 1066-5234. Pub. country: United States. Language: English.

AB Metacyclic trypomastigotes of Trypanosoma cruzi express a developmentally regulated 82 kDa surface glycoprotein (gp82) that has been implicated in the mammalian cell invasion. When the non-infective epimastigote stage of the parasite was transfected with a vector containing the gp82 gene, an 82 kDa surface glycoprotein, which was indistinguishable from the metacyclic stage protein, was expressed. In contrast, when the same gene was expressed in transfected mammalian cells, although a large amount of protein was produced, it was not imported into the endoplasmic reticulum and glycosylated. This blockage in targeting and processing could be partially compensated for by the addition of a virus haemagglutinin signal peptide to the amino terminus of gp82. Thus, the requirements for membrane protein processing are distinct in mammals and T. cruzi, and an intrinsic feature of the gp82 prevents subsequent sorting to the mammalian cell surface. These results could be useful in the development of new DNA vaccines against T. cruzi employing parasite genes encoding immunodominant surface glycoproteins.

L9 ANSWER 19 OF 30 MEDLINE on STN

1999375418. PubMed ID: 10446014. Heterologous expression of a trypanosoma cruzi surface glycoprotein (gp82) indicates that requirements for glycosylphosphatidylinositol anchoring are different in mammalian cells and this trypanosome. Ramirez M I; Boscardin S B; Ruiz R C; Han S W; **Paranhos-Baccala G S**; Yoshida N; Mortara R A; Silveira J F. (Departamento de Microbiologia, Imunologia e Parasitologia, Universidade Federal de Sao Paulo, Sao Paulo, SP, 04023-062, Brasil.) Memorias do Instituto Oswaldo Cruz, (1999 Jul-Aug) 94 (4) 527-30. Journal code: 7502619. ISSN: 0074-0276. Pub. country: Brazil. Language: English.

L9 ANSWER 20 OF 30 MEDLINE on STN

1999335590. PubMed ID: 10405350. Molecular cloning and characterization of MSRV-related sequences associated with retrovirus-like particles. Komurian-Pradel F; **Paranhos-Baccala G**; Bedin F; Ounanian-Paraz A; Sodoyer M; Ott C; Rajoharison A; Garcia E; Mallet F; Mandrand B; Perron H. (Ecole Normale Superieure de Lyon, UMR 103 CNRS-bioMerieux, 46, Allee d'Italie, Lyon Cedex 07, 69364, France.) Virology, (1999 Jul 20) 260 (1) 1-9. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB New sequences have been obtained by successive overlapping RT-PCR extensions from the pol region of a retroviral RNA (multiple

sclerosis-associated retroviral element, MSRV) amplified in retrovirus-like particles from patients with multiple sclerosis. gag and pol sequences are related to type C oncoviruses, whereas the env sequence is closer to type D. A tryptophan-like (W) tRNA primer-binding site was identified downstream of the RU5 region in the 5'LTR, and the U3R region cloned in the 3'LTR exhibited potent promoter activity. MSRV clones define a novel family of endogenous elements, HERV-W. From our data, HERV-W RNAs are copackaged in extracellular particles which might be produced by replication-competent or transcomplemented HERV-W copies or by an exogenous member of the HERV-W family.

L9 ANSWER 21 OF 30 MEDLINE on STN
1999045098. PubMed ID: 9829633. HCV core immunodominant region analysis using mouse monoclonal antibodies and human sera: characterization of major epitopes useful for antigen detection. Jolivet-Reynaud C; Dalbon P; Viola F; Yvon S; **Paranhos-Baccala G**; Piga N; Bridon L; Trabaud M A; Battail N; Sibai G; Jolivet M. (Departement des Immunoessais, bioMerieux, Marcy l'Etoile, France.. colette.jolivet@ensbma.cnrs.fr) . Journal of medical virology, (1998 Dec) 56 (4) 300-9. Journal code: 7705876. ISSN: 0146-6615. Pub. country: United States. Language: English.
AB Monoclonal antibodies (MAbs) were generated by immunizing mice with a truncated recombinant protein corresponding to the immunodominant region (residues 1-120) of hepatitis C virus (HCV) nucleocapsid protein. The specific recognition by either human sera or mouse monoclonal antibodies of overlapping peptides spanning the core region 1-120 as well as the comparison with epitopes described earlier allowed the fine mapping of HCV core. Within the region 1-120, the major antigenic domain could be restricted to the first 45 amino acids. Indeed, the peptide S42G (residues 2-45) allowed the detection of an anti-HCV core response by all anticore-positive human sera examined. According to their epitope localization, three groups of mouse MABs could be evidenced that were directed against different regions of core. Group II MAbs recognized a strictly linear epitope (QDVKF, residues 20-24), whereas group I MABs were directed against a conformational epitope mainly located at the amino acid residues (QIVGG, 29-33). The epitope of group III MABs was also conformational (PRGRRQPI, residues 58-65). These three epitopes appeared close but different from the three major human epitopes RKTKRNTN, VYLLPR, and GRTWAQPGYPWPLY (residues 7-17, 34-39, and 73-86, respectively). Group II MAB 7G12A8 and group I MAB 19D9D6 were used in a sandwich ELISA for the capture and the detection, respectively, of viral core antigen in sera of patients with chronic HCV infection. After treatment of sera with triton x 100 in acidic conditions, amounts of viral antigen as low as 20 pg/ml of sera could be detected.

L9 ANSWER 22 OF 30 MEDLINE on STN
1998095013. PubMed ID: 9433428. Detection of virion-associated MSRV-RNA in serum of patients with multiple sclerosis. Garson J A; Tuke P W; Giraud P; **Paranhos-Baccala G**; Perron H. Lancet, (1998 Jan 3) 351 (9095) 33. Journal code: 2985213R. ISSN: 0140-6736. Pub. country: ENGLAND: United Kingdom. Language: English.

L9 ANSWER 23 OF 30 MEDLINE on STN
1998022594. PubMed ID: 9359636. A cytotoxic factor for glial cells: a new avenue of research for multiple sclerosis?. Menard A; **Paranhos-Baccala G**; Pelletier J; Mandrand B; Seigneurin J M; Perron H; Reiger F. (INSERM, Laboratoire de Neuromodulations Interactives et Neuropathologies, Paris, France.) Cellular and molecular biology (Noisy-le-Grand, France), (1997 Sep) 43 (6) 889-901. Journal code: 9216789. ISSN: 0145-5680. Pub. country: France. Language: English.

AB A novel retrovirus, provisionally called Multiple Sclerosis RetroVirus (MSRV), was recently described in multiple sclerosis (MS). We report here that monocyte/macrophage culture supernatants from MS patients containing reverse transcriptase activity secrete a cytotoxin which induces death of primary mouse cortical glial cells. This cytotoxin, which was also found in MS cerebrospinal fluid, specifically causes death of mouse immortalized astrocytes and oligodendrocytes in vitro and seems to be associated to MSRV-specific RNA. This toxic factor, called gliotoxin, is present only in active cases of MS and is a stable glycosylated protein of 17 kDa, in CSF as well as in monocyte/macrophage culture supernatants. Since this gliotoxin is highly toxic for glial cells, it may represent an initial pathogenic factor, leading to the neuropathological features of MS, like blood brain barrier disruption and demyelination.

L9 ANSWER 24 OF 30 MEDLINE on STN

97391123. PubMed ID: 9247930. Cloning and characterization of a gene encoding a novel immunodominant antigen of Trypanosoma cruzi. Lesenechal M; Duret L; Cano M I; Mortara R A; Jolivet M; Camargo M E; da Silveira J F; **Paranhos-Baccala G.** (Unite Mixte CNRS-bio Merieux, Ecole Normale Superieure de Lyon, France.) Molecular and biochemical parasitology, (1997 Aug) 87 (2) 193-204. Journal code: 8006324. ISSN: 0166-6851. Pub. country: Netherlands. Language: English.

AB A Trypanosoma cruzi genomic expression library was screened with a pool of sera obtained from chronic chagasic patients. The recombinant antigen (Tc40) isolated from this library reacted with a large number of serum samples of chronic chagasic patients, suggesting that the presence of anti-Tc40 antibodies may be specifically associated to Chagas' disease. The full-length sequence of the Tc40 gene was determined after isolation of genomic and cDNA clones. The Tc40 cDNA includes a large open reading frame (2745 bp-long) that encodes a polypeptide of 100 kDa without any homology with previously described T. cruzi sequences. In contrast with other T. cruzi antigens whose immunodominant B-cell epitopes are composed by amino acid repetitive motifs, Tc40 does not show any amino acid repetition. Antibodies against the Tc40 recombinant protein reacted with three native polypeptides of 100, 41 and 38 kDa which are tightly associated with membranes or cytoskeleton and expressed in all developmental stages of the parasite life cycle. A transcript of 3.9-kb was detected in Northern blot analysis which is large enough to encode a 100 kDa polypeptide. Tc40 genes were mapped on a chromosomal band of 1.1 Mbp and in a few copies per haploid genome in the G strain.

L9 ANSWER 25 OF 30 MEDLINE on STN

97352842. PubMed ID: 9207135. Molecular identification of a novel retrovirus repeatedly isolated from patients with multiple sclerosis. The Collaborative Research Group on Multiple Sclerosis. Perron H; Garson J A; Bedin F; Beseme F; **Paranhos-Baccala G;** Komurian-Pradel F; Mallet F; Tuke P W; Voisset C; Blond J L; Lalande B; Seigneurin J M; Mandrand B. (bioMerieux SA, Unite Mixte de Recherche 103, Centre National de la Recherche Scientifique-bioMerieux, 46, Allee d'Italie, 69364 Lyon Cedex 07, France.) Proceedings of the National Academy of Sciences of the United States of America, (1997 Jul 8) 94 (14) 7583-8. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The partial molecular characterization of multiple sclerosis (MS)-associated retrovirus (MSRV), a novel retrovirus previously called LM7, is reported. MSRV has been isolated repeatedly from leptomeningeal, choroid plexus and from Epstein-Barr virus-immortalized B cells of MS patients. A strategy based on reverse transcriptase PCR with RNA-purified extracellular virions yielded an initial pol fragment from which other regions of the retroviral genome were subsequently obtained by sequence extension. MSRV-specific PCR primers amplified a pol region from RNA

present at the peak of reverse transcriptase activity, coinciding with extracellular viral particles in sucrose density gradients. The same sequence was detected in noncellular RNA from MS patient plasma and in cerebrospinal fluid from untreated MS patients. MSRV is related to, but distinct from, the endogenous retroviral sequence ERV9. Whether MSRV represents an exogenous retrovirus with closely related endogenous elements or a replication-competent, virion-producing, endogenous provirus is as yet unknown. Further molecular epidemiological studies are required to determine precisely the apparent association of virions containing MSRV RNA with MS.

L9 ANSWER 26 OF 30 MEDLINE on STN

96178593. PubMed ID: 8606064. A recombinant protein based on the Trypanosoma cruzi metacyclic trypomastigote 82-kilodalton antigen that induces and effective immune response to acute infection. Santori F R; **Paranhos-Bacalla G S**; Franco DA Silveira J; Yamauchi L M; Araya J E; Yoshida N. (Departamento de Microbiologia, Immunologia e Parasitologia, Escola Paulista de Medicina, Universidade Federal de Sao Paulo, Brazil.) Infection and immunity, (1996 Apr) 64 (4) 1093-9. Journal code: 0246127. ISSN: 0019-9567. Pub. country: United States. Language: English.

AB To further investigate the immunological properties of the stage-specific 82-kDa glycoprotein (gp82) of Trypanosoma cruzi metacyclic trypomastigotes, previously shown to induce antigen-specific humoral and T-cell responses in mice, we performed a series of experiments with recombinant proteins containing sequences of gp82 fused to glutathione S-transferase. Of five fusion proteins tested, only J18b and J18b1, the carboxyproximal peptides containing amino acids 224 to 516 and 303 to 516, respectively, were recognized by monoclonal antibody 3F6 as well as by various anti-T. cruzi antisera and, when administered to mice, were capable of eliciting antibodies directed to the native gp82. The amino-terminal peptide and other carboxyterminal recombinant proteins lacking the central domain of gp82 (amino acids 224 to 356), which is exposed on the surface of live metacyclic forms, did not display any of these properties. Spleen cells derived from mice immunized with any of the five recombinant proteins proliferated in vitro in the presence of native gp82.J18b was the most stimulatory, whereas J18b3, the peptide containing amino acids 408 to 516, elicited the weakest response. When BALB/c mice immunized with J18b antigen plus Al(OH)3 as adjuvant were challenged 10 5 metacyclic trypomastigotes, 85% of them resisted acute infection, in comparison with control mice that received glutathione S-transferase plus adjuvant. Antibodies induced by J18b protein lacked agglutinating or complement-dependent lytic activity and failed to neutralize parasite infectivity. On the other hand, CD4+T cells from the spleens of J18b-immunized mice displayed an intense proliferative activity upon stimulation with 1.25 microgram of native gp82 per ml, which resulted in increased production of gamma interferon, a cytokine associated with resistance to T. cruzi infection.

L9 ANSWER 27 OF 30 MEDLINE on STN

95356800. PubMed ID: 7630386. Organization and expression of the gene encoding an immunodominant repetitive antigen associated to the cytoskeleton of Trypanosoma cruzi. Cotrim P C; **Paranhos-Baccala G**; Santos M R; Mortensen C; Cano M I; Jolivet M; Camargo M E; Mortara R A; Da Silveira J F. (Department of Microbiology, Immunology and Parasitology, Escola Paulista de Medicina, Sao Paulo, Brazil.) Molecular and biochemical parasitology, (1995 Apr) 71 (1) 89-98. Journal code: 8006324. ISSN: 0166-6851. Pub. country: Netherlands. Language: English.

AB We have studied the genomic organization and expression of the gene encoding a high molecular mass (300 kDa) repetitive antigen associated with the cytoskeleton of Trypanosoma cruzi. Protease digestion of the

native protein, restriction analysis of genomic DNA and sequencing of genomic and cDNA clones indicated that most of the protein is built up by tandemly arranged, nearly identical repeats of 68 amino acids. The gene size was estimated to be approx. 9.4 kb based on the sizes of the transcript and the native protein. The nucleotide sequence conservation among the repeats indicates that selective sequence homogenization, presumably through gene conversion, maintained the amino-acid sequence conservation. Two duplicated allelic forms of this gene were mapped in fragments of about 20 kb. In some strains an additional allele was located in a fragment of 9.4 kb. Our results suggest that this repetitive antigen is a structural protein which could be involved in the attachment of the flagellum to the cell body.

L9 ANSWER 28 OF 30 MEDLINE on STN

95194868. PubMed ID: 7534103. Major antigenic epitopes of bullous pemphigoid 230 kDa antigen map within the C-terminal end of the protein. Evidence using a 55 kDa recombinant protein. Gaucherand M; Nicolas J F; **Paranhos Baccala G**; Rouault J P; Reano A; Magaud J P; Thivolet J; Jolivet M; Schmitt D. (Inserm 346, Clinique Dermatologique, Universite Claude Bernard Lyon I, Hopital Edouard Y Herriot, France.) British journal of dermatology, (1995 Feb) 132 (2) 190-6. Journal code: 0004041. ISSN: 0007-0963. Pub. country: ENGLAND: United Kingdom. Language: English.

AB In order to obtain greater insight into the nature of B-cell epitopes in bullous pemphigoid (BP), we generated a BP recombinant protein of 55 kDa M(r) (rBP 55) from a cDNA sequence encoding for the carboxyterminal region of the 230 kDa BP antigen. Serum IgG from guinea-pigs immunized with rBP 55 stained the basement membrane zone of normal human skin and immunoprecipitated the rBP 55 protein, and also the 230 kDa BP antigen recovered from extracts of cultured keratinocytes, thus confirming that the rBP 55 amino acid sequence is present in native BP antigen. The reactivity of sera from 60 patients with BP was analysed using an immunoblot assay on epidermal protein extracts and on the rBP 55 protein. Forty of the 60 BP sera (66%) contained autoantibodies to the 230 kDa polypeptide in an epidermal extract, and 37 of these 40 sera (92%) recognized the rBP 55 protein. In contrast, no reactivity against rBP 55 was detected with 20 BP sera devoid of autoantibodies against the 230 kDa antigen. Likewise, sera from patients with autoimmune blistering skin disorders other than BP (epidermolysis bullosa acquisita or pemphigus vulgaris), and control sera, were unreactive to rBP 55. These results clearly demonstrate the immunogenicity and antigenicity of the C-terminal end of the 230 kDa BP antigen. They confirm that this 555 amino acid segment, corresponding to rBP 55, contains major epitopes which can bind BP patients' autoantibodies, and suggest that the rBP 55 protein could be useful for further characterization of these B-cell epitopes.

L9 ANSWER 29 OF 30 MEDLINE on STN

94268886. PubMed ID: 8208589. Detection of antibodies in sera from Chagas' disease patients using a Trypanosoma cruzi immunodominant recombinant antigen. **Paranhos-Bacalla G S**; Santos M R; Cotrim P C; Rassi A; Jolivet M; Camargo M E; Da Silveira J F. (Bio-Merieux, Lyon, France; Biolab Diagnostica, Sao Paulo, Brasil.) Parasite immunology, (1994 Mar) 16 (3) 165-9. Journal code: 7910948. ISSN: 0141-9838. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A Trypanosoma cruzi DNA fragment encoding an immunodominant repetitive antigen (H49) was subcloned into a protein purification and expressed system. Purified H49 peptide reacted specifically in an enzyme-linked immunosorbent assay (ELISA) with sera from T. cruzi-infected patients, but not with sera from patients with other parasitic diseases such as leishmaniasis and T. rangeli-infection. The H49 recombinant ELISA was able to detect specific antibodies in 84% of chronic chagasic serum

samples tested. One of the major advantage of the recombinant ELISA for serodiagnosis of chronic Chagas' disease resides in its high specificity (100%). Our data suggest that recombinant peptides could provide a practical basis for specific diagnosis tests for Chagas' disease.

L9 ANSWER 30 OF 30 MEDLINE on STN
94011305. PubMed ID: 8406808. Characterization of a cDNA clone encoding the carboxy-terminal domain of a 90-kilodalton surface antigen of Trypanosoma cruzi metacyclic trypomastigotes. Franco F R; **Paranhos-Bacalla G S**; Yamauchi L M; Yoshida N; da Silveira J F. (Department of Microbiology, Immunology and Parasitology, Escola Paulista de Medicina, Sao Paulo, Brazil.) Infection and immunity, (1993 Oct) 61 (10) 4196-201. Journal code: 0246127. ISSN: 0019-9567. Pub. country: United States. Language: English.
AB We have cloned and sequenced a cDNA for a metacyclic trypomastigote-specific glycoprotein with a molecular mass of 90 kDa, termed MTS-gp90. By immunoblotting, antibodies to the MTS-gp90 recombinant protein reacted exclusively with a 90-kDa antigen of metacyclic trypomastigotes. The insert of the MTS-gp90 cDNA clone strongly hybridized with a single 3.0-kb mRNA of metacyclic forms, whereas the hybridization signal with epimastigote mRNA was weak and those with RNAs from other developmental stages were negative, indicating that transcription of the MTS-gp90 gene is developmentally regulated. A series of experiments showed that the MTS-gp90 gene is present in multiple copies in the Trypanosoma cruzi genome, arranged in a nontandem manner, and that there are at least 40 copies of the gene per haploid genome. Sequence analysis of recombinant MTS-gp90 revealed 40 to 60% identity at the amino acid level with members of a family of mammalian stage-specific, 85-kDa surface antigens of T. cruzi. However, there are considerable differences in the amino acid compositions outside the homology region.

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=> e perron h/au
E1            1     PERRON GINO/AU
E2            1     PERRON GREGORY A/AU
E3           37 --> PERRON H/AU
E4            1     PERRON H J/AU
E5            1     PERRON HENRY D/AU
E6            8     PERRON HENRY D M/AU
E7            2     PERRON HERVE/AU
E8           41     PERRON J/AU
E9            2     PERRON J C/AU
E10           1     PERRON J E/AU
E11           1     PERRON J J/AU
E12           6     PERRON J L/AU

=> s e3 or e7
             37 "PERRON H"/AU
              2 "PERRON HERVE"/AU
L10          39 "PERRON H"/AU OR "PERRON HERVE"/AU

=> s l10 not l9
L11          34 L10 NOT L9

=> d l11,cbib,ab,1-34

L11 ANSWER 1 OF 34     MEDLINE on STN
2005162111.    PubMed ID: 15794403.   MSRV, Syncytin and the role of endogenous
     retroviral proteins in demyelination. Garson J; Creange A; Dolei A;
     Ferrante P; Jouvin-Marche E; Marche P N; Rieger F; Ruprecht K; Saresella
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M; Sotgiu S; Tedder R; **Perron H**. Multiple sclerosis (Houndmills, Basingstoke, England), (2005 Apr) 11 (2) 249-50. Journal code: 9509185. ISSN: 1352-4585. Pub. country: England: United Kingdom. Language: English.

L11 ANSWER 2 OF 34 MEDLINE on STN

2005082131. PubMed ID: 15710473. Correlation between disease severity and in vitro cytokine production mediated by MSRV (Multiple Sclerosis associated RetroViral element) envelope protein in patients with multiple sclerosis. Rolland Alexandre; Jouvin-Marche Evelyne; Saresella Marina; Ferrante Pasquale; Cavaretta Rosella; Creange Alain; Marche Patrice; **Perron Herve**. (Laboratoire d'Immunochimie, CEA/ INSERM-U548, 17 rue des Martyrs 38054 Grenoble, France.) Journal of neuroimmunology, (2005 Mar) 160 (1-2) 195-203. Electronic Publication: 2004-12-08. Journal code: 8109498. ISSN: 0165-5728. Pub. country: Netherlands. Language: English.

AB MSRV is a retroviral element previously isolated in cell cultures from patients with multiple sclerosis. It is part of a new multi-copy endogenous retrovirus family named HERV-W and displays pro-inflammatory properties both in vitro in human PBMC cultures and in vivo in a humanized SCID mice model. In the present study, we have evaluated potential links between the pro-inflammatory properties of MSRV envelope protein and MS disease. Thus, cytokine productions mediated by the surface unit of MSRV envelope protein were evaluated in PBMC of MS patients and compared with healthy controls. Divergent reactivity to ENV-SU between MS and control PBMC was observed and was reflected by a significant increase of IFN-gamma, IL-6 and IL-12p40 production by the tested MS population. Interestingly, the overproduction of IL-6 and IL-12p40 was found to correlate with disease severity (EDSS) in most patients. Altogether our data suggest that MSRV envelope protein may induce an abnormal cytokine secretion, thus contributing to the inflammatory process in MS.

L11 ANSWER 3 OF 34 MEDLINE on STN

2003143214. PubMed ID: 12587071. Multiple sclerosis-associated retrovirus particles cause T lymphocyte-dependent death with brain hemorrhage in humanized SCID mice model. Firouzi R; Rolland A; Michel M; Jouvin-Marche E; Hauw J J; Malcus-Vocanson C; Lazarini F; Gebuhrer L; Seigneurin J M; Touraine J L; Sanhadji K; Marche P N; **Perron H**. (Laboratoire des deficits Immunitaires, Faculte de Medecine Laennec, Lyon, France.) Journal of neurovirology, (2003 Feb) 9 (1) 79-93. Journal code: 9508123. ISSN: 1355-0284. Pub. country: United States. Language: English.

AB A retroviral element (multiple sclerosis-associated retrovirus, MSRV) defining a family of genetically inherited endogenous retroviruses (human endogenous retrovirus type W, HERV-W) has been characterized in cell cultures from patients with multiple sclerosis. Recently, MSRV retroviral particles or the envelope recombinant protein were shown to display superantigen activity in vitro, but no animal model has yet been set up for studying the pathogenicity of this retrovirus. In the present study, the pathogenicity of different sources of MSRV retroviral particles has been evaluated in a hybrid animal model: severe combined immunodeficiency (SCID) mice grafted with human lymphocytes and injected intraperitoneally with MSRV virion or mock controls. MSRV-injected mice presented with acute neurological symptoms and died within 5 to 10 days post injection. Necropsy revealed disseminated and major brain hemorrhages, whereas control animals did not show abnormalities (P <.001). In ill animals, reverse transcriptase-polymerase chain reaction (RT-PCR) analyses showed circulating MSRV RNA in serum, whereas overexpression of proinflammatory cytokines such as tumor necrosis factor (TNF)-alpha and interferon (IFN)-gamma was evidenced in spleen RNA. Neuropathological examination confirmed that hemorrhages occurred prior to death in multifocal areas of brain parenchyma and meninges. Further series addressed the question of immune-mediated pathogenicity, by inoculating virion to SCID mice grafted

with total and T lymphocyte-depleted cells in parallel: dramatic and statistically significant reduction in the number of affected mice was observed in T-depleted series (P <.001). This in vivo study suggests that MSRV retroviral particles from MS cultures have potent immunopathogenic properties mediated by T cells compatible with the previously reported superantigen activity in vitro, which appear to be mediated by an overexpression of proinflammatory cytokines.

L11 ANSWER 4 OF 34 MEDLINE on STN
2002357851. PubMed ID: 12102742. Human viral superantigens: to be or not to be transactivated?. Lafon Monique; Jouvin-Marche Evelyne; Marche Patrice N; **Perron Herve**. Trends in immunology, (2002 May) 23 (5) 238-9; author reply 239. Journal code: 100966032. ISSN: 1471-4906. Pub. country: England: United Kingdom. Language: English.

L11 ANSWER 5 OF 34 MEDLINE on STN
2002069249. PubMed ID: 11795460. Glial toxicity in urine and multiple sclerosis. Malcus-Vocanson C; Giraud P; Micoud F; Janin V; Charles M H; Broussolle E; Chazot G; Mandrand B; **Perron H**. (bioMerieux-Pierre Fabre, Marcy L'Etoile, France.) Multiple sclerosis (Houndmills, Basingstoke, England), (2001 Dec) 7 (6) 383-8. Journal code: 9509185. ISSN: 1352-4585. Pub. country: England: United Kingdom. Language: English.
AB The biochemical and biological characterization of a cytotoxic activity targeting macroglial cells (oligodendrocytes and astrocytes), in moncyte cultures and in CSF of a patient with multiple sclerosis, has previously been described. In further studies, cell-based tests have shown a good correlation between this glial cytotoxic (gliotoxic) activity, in CSF or in urine, and MS. We now present results obtained with urine samples from 102 MS patients, 51 patients with other neurological disease and 35 healthy subjects using a bioassay set up for the detection of an apoptosis-like effect induced in a glial cell-line. Significant gliotoxicity was detected in urine from 74/102 MS patients while only 4/51 neurological controls (P>0.001) and never in healthy subjects (P>0.001). Given the statistical tendency provided by this bioassay and its technical limitations for routine testing, it is now used for monitoring the molecular characterization of this 'gliotoxic factor'. Its replacement by a specific immunoassay could provide more accurate routine techniques for the detection of this biological marker in MS.

L11 ANSWER 6 OF 34 MEDLINE on STN
2001491405. PubMed ID: 11531410. Multiple sclerosis retrovirus particles and recombinant envelope trigger an abnormal immune response in vitro, by inducing polyclonal Vbeta16 T-lymphocyte activation. **Perron H**; Jouvin-Marche E; Michel M; Ounanian-Paraz A; Camelo S; Dumon A; Jolivet-Reynaud C; Marcel F; Souillet Y; Borel E; Gebuhrer L; Santoro L; Marcel S; Seigneurin J M; Marche P N; Lafon M. (BioMerieux-Pierre Fabre, R&D, Chemin de L'Orme, Marcy L'Etoile, 69280, France.. herve_perron@eu.biomerieux.com) . Virology, (2001 Sep 1) 287 (2) 321-32. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.
AB A retroviral element (MSRV) defining a family of genetically inherited endogenous retroviruses (HERV-W) has recently been characterized in cell cultures from patients with multiple sclerosis (MS). To address the possible relationship with MS, direct detection of circulating virion RNA was proposed but revealed technically difficult to perform in standardized conditions, in the face of multiple endogenous HERV-W copies. A parallel approach has evaluated MSRV potential pathogenicity in relation to characteristic features of multiple sclerosis, in particular, T-lymphocyte-mediated immunopathology. We report here that MSRV particles induce T-lymphocyte response with a bias in the Vbeta16 chain usage in

surface receptor, whatever the HLA DR of the donor. A recombinant MSRV envelope-but not core-protein reproduced similar nonconventional activation. Molecular analysis of Vbeta CDR3 showed that Vbeta16 expansions are polyclonal. Our results thus provide evidence that MSRV envelope protein can trigger an abnormal immune response with similar characteristics to that of superantigens.

L11 ANSWER 7 OF 34 MEDLINE on STN
2001072824. PubMed ID: 10602665. Human retroviral sequences associated with extracellular particles in autoimmune diseases: epiphenomenon or possible role in aetiopathogenesis?. **Perron H**; Seigneurin J M. (BioMerieux SA, Chemin de l'Orme 69280 Marcy l'Etoile, France.) Microbes and infection / Institut Pasteur, (1999 Apr) 1 (4) 309-22. Ref: 64. Journal code: 100883508. ISSN: 1286-4579. Pub. country: France. Language: English.
AB Publications describing retroviral sequences associated with extracellular particles in Sjogren's syndrome or systemic lupus erythematosus, multiple sclerosis, and type I diabetes present novel arguments and raise complex questions about eventual relationships between retroviruses and autoimmunity. They are presented and discussed in the present review, preceded by an overview of the biology of retroviral elements.

L11 ANSWER 8 OF 34 MEDLINE on STN
2001030746. PubMed ID: 10986298. Infrequency of detection of particle-associated MSRV/HERV-W RNA in the synovial fluid of patients with rheumatoid arthritis. Gaudin P; Ijaz S; Tuke P W; Marcel F; Paraz A; Seigneurin J M; Mandrand B; **Perron H**; Garson J A. (Department of Virology, Royal Free and University College Medical School, London, UK.) Rheumatology (Oxford, England), (2000 Sep) 39 (9) 950-4. Journal code: 100883501. ISSN: 1462-0324. Pub. country: ENGLAND: United Kingdom. Language: English.
AB OBJECTIVES: To determine whether the recently identified multiple sclerosis-associated retrovirus, MSRV, is detectable in the serum and synovial fluid of patients with rheumatoid arthritis (RA). METHODS: A reverse transcription-polymerase chain reaction (RT-PCR) assay was used to seek evidence of particle-associated MSRV/HERV-W RNA in the plasma and synovial fluid of patients with RA and controls. Stringent precautions were taken to avoid detection of contaminating human genomic DNA and cellular RNA sequences. RESULTS: Thirty-seven plasma samples were tested (20 from RA patients and 17 from controls) but none had detectable MSRV/HERV-W RNA. Synovial fluid samples were available from nine patients with RA and 10 controls. Particle-associated MSRV/HERV-W RNA was reproducibly detected in two of nine synovial fluid samples from RA patients and in one control sample. The identity of RT-PCR products was confirmed by sequencing. CONCLUSION: MSRV/HERV-W RNA sequences are detectable in the synovial fluid of a small proportion of RA patients, but this phenomenon may not be specific to RA.

L11 ANSWER 9 OF 34 MEDLINE on STN
2000332466. PubMed ID: 10871789. Particle-associated retroviral RNA and tandem RGH/HERV-W copies on human chromosome 7q: possible components of a 'chain-reaction' triggered by infectious agents in multiple sclerosis?. **Perron H**; Perin J P; Rieger F; Alliel P M. (BioMerieux STELHYS, Chemin de l'Orme, 69280 Marcy l'Etoile, France.) Journal of neurovirology, (2000 May) 6 Suppl 2 S67-75. Ref: 33. Journal code: 9508123. ISSN: 1355-0284. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Different groups have observed retrovirus particle (RVP) production in cell cultures from patients with multiple sclerosis (MS). This in vitro production appeared relatively specific for MS versus healthy controls,

but was likely to be enhanced or activated by infectious triggers such as Herpesviruses (e.g. HSV, EBV). Independent molecular analysis of retroviral RNA associated with RVP revealed two different genetic families of endogenous retroviral elements (HERV): MSRV/HERV-W and RGH/HERV-H. Interestingly, these sequences were detected by mutually exclusive primers in RT - PCR amplifications. Surprisingly, these two HERV families both contain an ancestral proviral copy inserted in chromosome 7q21-22 region at about 1 kb of distance of each other. Another HERV-W proviral sequence is located within a T-cell alpha-delta receptor (TCR) gene in chromosome 14q11.2 region. Interestingly, these two regions correspond to genetic loci previously identified as potentially associated with 'multigenic' susceptibility to MS and TCR alpha chain genetic determinants have been reported to be statistically associated with MS. A plausible role for infectious agents triggering a co-activation of the chromosome 7q HERV tandem (replicative retrovirus and/or other virus and/or intracellular bacteria) and, eventually, other HERV copies, is discussed. The role of particular HERV polymorphism and the production of pathogenic molecules (gliotoxin and superantigen) possibly associated with retroviral expression are also evoked. An integrative concept of pathogenic 'chain-reaction' in MS involving several step-specific pathogenic 'agents' and 'products' somewhat interacting with particular genetic elements would federate most partial data obtained on MS, including retroviral expression.

L11 ANSWER 10 OF 34 MEDLINE on STN
2000071226. PubMed ID: 10600340. Specificities of multiple sclerosis cerebrospinal fluid and serum antibodies against mimotopes. Jolivet-Reynaud C; **Perron H**; Ferrante P; Becquart L; Dalbon P; Mandrand B. (Unite Mixte de Recherche 103, Centre National de la Recherche Scientifique-bioMerieux, 46 Allee d'Italie, Lyon Cedex 07, 69364, France.. Colette.Jolivet@ens-bma.cnrs.fr) . Clinical immunology (Orlando, Fla.), (1999 Dec) 93 (3) 283-93. Journal code: 100883537. ISSN: 1521-6616. Pub. country: United States. Language: English.

AB In order to characterize antigenic epitopes specifically targeted by the immune response of patients with multiple sclerosis (MS), the antibody specificities of cerebrospinal fluids (CSF) and sera from the same MS patients have been analyzed using a random pentadecapeptide library displayed on phage. The 3 peptides (mimotopes) selected with MS sera were not disease-specific. In contrast, the combination of 4 MS CSF selected mimotopes, allowed the detection of specific antibodies in 21 of 60 MS CSF whereas only 2 of 27 CSF from patients with other neurological diseases equally recognized the 4 mimotopes. Some amino acid similarities were found between two MS CSF selected mimotopes and two envelope regions (319-329 and 433-443, respectively) of MSRV (multiple-sclerosis-associated retrovirus) and the related endogenous retrovirus HERV-W.

L11 ANSWER 11 OF 34 MEDLINE on STN
1999099005. PubMed ID: 9882319. Molecular characterization and placental expression of HERV-W, a new human endogenous retrovirus family. Blond J L; Beseme F; Duret L; Bouton O; Bedin F; **Perron H**; Mandrand B; Mallet F. (Unite Mixte 103 CNRS-bioMerieux, Ecole Normale Superieure de Lyon, 69364 Lyon, Cedex 07, France.) Journal of virology, (1999 Feb) 73 (2) 1175-85. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The multiple sclerosis-associated retrovirus (MSRV) isolated from plasma of MS patients was found to be phylogenetically and experimentally related to human endogenous retroviruses (HERVs). To characterize the MSRV-related HERV family and to test the hypothesis of a replication-competent HERV, we have investigated the expression of

MSRV-related sequences in healthy tissues. The expression of MSRV-related transcripts restricted to the placenta led to the isolation of overlapping cDNA clones from a cDNA library. These cDNAs spanned a 7.6-kb region containing gag, pol, and env genes; RU5 and U3R flanking sequences; a polypurine tract; and a primer binding site (PBS). As this PBS showed similarity to avian retrovirus PBSs used by tRNATrp, this new HERV family was named HERV-W. Several genomic elements were identified, one of them containing a complete HERV-W unit, spanning all cDNA clones. Elements of this multicopy family were not replication competent, as gag and pol open reading frames (ORFs) were interrupted by frameshifts and stop codons. A complete ORF putatively coding for an envelope protein was found both on the HERV-W DNA prototype and within an RU5-env-U3R polyadenylated cDNA clone. Placental expression of 8-, 3.1-, and 1.3-kb transcripts was observed, and a putative splicing strategy was described. The apparently tissue-restricted HERV-W long terminal repeat expression is discussed with respect to physiological and pathological contexts.

L11 ANSWER 12 OF 34 MEDLINE on STN

1998426886. PubMed ID: 9754278. [MSRV retrovirus and gliotoxin protein: potential biological markers in multiple sclerosis?]. Retrovirus MSRV et proteine gliotoxique: marqueurs biologiques potentiels dans la sclerose en plaques?. **Perron H.** (Unite mixte CNRS-bioMerieux, Lyon.) Annales de biologie clinique, (1998 Jul-Aug) 56 (4) 427-38. Ref: 52. Journal code: 2984690R. ISSN: 0003-3898. Pub. country: France. Language: French.

AB The aetiopathogeny of multiple sclerosis, a neurological disease which prevalence and duration generate an important problem of public health in industrialized countries where it is most frequent, is not clearly understood. The keys for the diagnosis and therapeutic strategies of MS are nonetheless dependent upon the identification of a well-defined aetiology and upon the understanding of the mechanisms and pathogenic connexions which lead to the demyelinating lesions of the central nervous system and to the dysfunctions of the immune system (autoimmunity) characteristic for the disease. The recent identification of a retroviral agent (MSRV) which produces extracellular particles detectable in the plasma, the CSF, and in some cell cultures from patients with MS, as well as of a cytotoxic factor targeting glial cells (gliotoxin) detected in parallel, could help elucidating the aetiopathogeny of MS. The usefulness of biological markers and targets derived from MSRV retrovirus and this gliotoxin, in the diagnostic and therapeutic perspectives for MS, is discussed in the light of the different aetiopathogenic hypotheses for the disease. From our results it is conceivable that a retroviral agent and pathogenic molecules such as this gliotoxin and an eventual MSRV-associated retroviral superantigen might initiate and perpetuate the cascade of events leading to MS. However, similar data on different simple retroviruses were recently published concerning autoimmune diseases such as diabetes type 1, Sjogren's syndrome and systemic lupus erythematosis, which could prefigurate a broader concept for the role of such retroviruses in the aetiopathogenesis of autoimmune diseases.

L11 ANSWER 13 OF 34 MEDLINE on STN

1998342032. PubMed ID: 9678892. Case report: DNA fragmentation in glial cells in a cerebral biopsy from a multiple sclerosis patient. Benjelloun N; Menard A; Charriaut-Marlangue C; Mokhtari K; **Perron H**; Hauw J J; Rieger F. (INSERM, Laboratoire de Neuromodulations Interactives et Neuropathologies, Paris, France.) Cellular and molecular biology (Noisy-le-Grand, France), (1998 Jun) 44 (4) 579-83. Journal code: 9216789. ISSN: 0145-5680. Pub. country: France. Language: English.

AB Multiple sclerosis is characterized by myelin destruction and oligodendrocyte loss. The neuropathological hallmark of the disease is the presence of demyelinated plaques in the central nervous system. We

have recently found a gliotoxic factor in MS cerebrospinal fluid which induces programmed cell death in vitro, in glial cells. Here we show DNA fragmentation and glial cell death in biopsy samples, obtained from a patient who underwent surgery with suspicion of tumor, and whose disease record, including brain autopsy, demonstrated an active multiple sclerosis. We used the in situ TUNEL technique, a method which sensitively detects the DNA fragmentation accompanying programmed cell death in tissue sections, and compatible with classical fixation techniques. We found intense DNA fragmentation in nuclei of glial cells at-or very near-to the site of demyelination. A double labeling technique showed that glial fibrillary associated protein positive astrocytes may undergo programmed cell death in multiple sclerosis.

L11 ANSWER 14 OF 34 MEDLINE on STN
1998305954. PubMed ID: 9643801. A urinary marker for multiple sclerosis. Malcus-Vocanson C; Giraud P; Broussolle E; **Perron H**; Mandrand B; Chazot G. Lancet, (1998 May 2) 351 (9112) 1330. Journal code: 2985213R. ISSN: 0140-6736. Pub. country: ENGLAND: United Kingdom. Language: English.

L11 ANSWER 15 OF 34 MEDLINE on STN
1998255792. PubMed ID: 9596353. Detection of a gliotoxic activity in the cerebrospinal fluid from multiple sclerosis patients. Menard A; Pierig R; Pelletier J; Bensa P; Belliveau J; Mandrand B; **Perron H**; Rieger F. (INSERM Laboratoire de Neuromodulations Interactives et Neuropathologies - 17, Paris, France.) Neuroscience letters, (1998 Mar 27) 245 (1) 49-52. Journal code: 7600130. ISSN: 0304-3940. Pub. country: Ireland. Language: English.
AB We recently showed that peripheral blood cell supernatants from multiple sclerosis (MS) patients, containing reverse transcriptase activity and retroviral RNA from the newly human identified multiple sclerosis retrovirus (MSRV), also secrete a cytotoxin which induces death of primary mouse cortical glial cells. We have hypothesized that macrophages could release this cytotoxin in the cerebrospinal fluid. The cerebrospinal fluid cytotoxicity from 166 patients with various neurological diseases (including MS patients) was tested on glial cells in vitro. Our bioassay shows that a glial cytotoxic activity is significantly present in cerebrospinal fluid from patients with relapsing-remitting MS at relapse. Since this cytotoxic activity seems to correlate with active cases of MS, it may represent a critical pathogenic factor in the neuropathology of MS.

L11 ANSWER 16 OF 34 MEDLINE on STN
1998220782. PubMed ID: 9562313. A gliotoxic factor and multiple sclerosis. Menard A; Amouri R; Dobransky T; Charriaut-Marlangue C; Pierig R; Cifuentes-Diaz C; Ghandour S; Belliveau J; Gascan H; Hentati F; Lyon-Caen O; **Perron H**; Rieger F. (INSERM, Laboratoire de Neuromodulations Interactives et Neuropathologies, Paris, France.) Journal of the neurological sciences, (1998 Feb 5) 154 (2) 209-21. Journal code: 0375403. ISSN: 0022-510X. Pub. country: Netherlands. Language: English.
AB The pathogenesis of multiple sclerosis (MS) is unknown. Searching for possible toxic factors, it was found that 3-day exposure to heat-treated cerebrospinal fluid (CSF) from MS patients caused apoptotic death of astrocytes and oligodendrocytes, but not fibroblasts, myoblasts, Schwann cells, endothelial cells and neurons, in vitro. CSFs from other inflammatory or non-inflammatory neurological diseases showed no toxicity. Exposure of these glial cells to partially purified MS CSF produced DNA fragmentation, apoptotic bodies, chromatin condensation, cell shrinkage, and changes in the levels of known cytokines. A cytotoxic factor, called gliotoxin, was characterized chromatographically as a stable 17-kDa glycoprotein. Since this protein is highly cytotoxic for astrocytes and oligodendrocytes, it may represent an initial pathogenic factor, leading

to the neuropathological features of MS, such as blood-brain barrier involvement and demyelination.

L11 ANSWER 17 OF 34 MEDLINE on STN
1998005317. PubMed ID: 9345457. Expression of endogenous retroviruses in blood mononuclear cells and brain tissue from multiple sclerosis patients. Rasmussen H B; Geny C; Deforges L; **Perron H**; Tourtelotte W; Heltberg A; Clausen J. (Institute of Life Sciences and Chemistry, Roskilde University, Denmark.) Multiple sclerosis (Houndmills, Basingstoke, England), (1995 Jun) 1 (2) 82-7. Journal code: 9509185. ISSN: 1352-4585. Pub. country: ENGLAND: United Kingdom. Language: English.
AB The aim of the present study was to examine whether there is an abnormal expression of certain endogenous retroviruses in MS patients. For this purpose samples of peripheral blood mononuclear cells were obtained from 22 MS patients, a corresponding number of age and sex-matched healthy donors and five patients with other diseases affecting the central nervous system. In addition, brain specimens of macroscopic normal white and gray matter from four MS patients and a similar number of controls were included in the study. Using an enzymatic amplification technique, we found expression of the endogenous retroviral sequences, HRES-1, HERV-K10 and ERV3 in most samples of peripheral blood mononuclear cells from MS patients and controls without obvious differences between these two groups. In contrast, composite transcripts of ERV3 and a zinc finger sequence were more frequently detected in healthy donors than in MS patients. At present, the possible significance of this is uncertain. The retroviral element 4-1 was not transcribed or only transcribed at a very low level in peripheral blood cells of controls and MS patients. Transcripts of various endogenous retroviruses were also detected in the brain samples, but a different pattern was not apparent in the MS group as compared with controls. Aspects concerning a possible association between endogenous retroviruses and autoimmunity are considered.

L11 ANSWER 18 OF 34 MEDLINE on STN
97447819. PubMed ID: 9303559. Gliotoxicity, reverse transcriptase activity and retroviral RNA in monocyte/macrophage culture supernatants from patients with multiple sclerosis. Menard A; Amouri R; Michel M; Marcel F; Brouillet A; Belliveau J; Geny C; Deforges L; Malcus-Vocanson C; Armstrong M; Lyon-Caen O; Mandrand B; Dobransky T; Rieger F; **Perron H**. (INSERM, Laboratoire de Neuromodulations Interactives et Neuropathologies, Paris, France.) FEBS letters, (1997 Aug 25) 413 (3) 477-85. Journal code: 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.
AB In investigating a possible link between a novel retroviral agent (provisionally called MSRV), recently characterised in multiple sclerosis (MS), and the neuropathology of MS, it was found that there was a significant correlation between gliotoxicity and reverse transcriptase activity in monocyte/macrophage culture supernatants (MMCS) unique to MS patients. MMCS from healthy controls and patients with other neurological diseases did not display either gliotoxicity or reverse transcriptase activity. The observed gliotoxic effect was an initial, intermediate filament network disorganization and subsequent cell death which was specific to astrocytes and oligodendrocytes. The reverse transcriptase activity and MSRV-specific RNA were observed during the first 2 weeks of culture in MMCS from patients with active MS. The further elucidation of the molecular form(s) of this gliotoxic factor and its original source may be crucial in elucidating important etiopathogenic mechanisms in MS.

L11 ANSWER 19 OF 34 MEDLINE on STN
97317644. PubMed ID: 9174639. Expression of endogenous retroviruses in blood mononuclear cells and brain tissue from multiple sclerosis patients. Rasmussen H B; Geny C; Deforges L; **Perron H**; Tourtelotte W; Heltberg A;

Clausen J. (Institute of Life Sciences and Chemistry, Roskilde University, Denmark.) Acta neurologica Scandinavica. Supplementum, (1997) 169 38-44. Journal code: 0370337. ISSN: 0065-1427. Pub. country: Denmark. Language: English.

AB OBJECTIVES: To compare the expression of endogenous retroviruses in MS patients and controls. MATERIAL AND METHODS: Peripheral blood mononuclear cells were obtained from 22 MS patients, a corresponding number of matched healthy donors and five patients with other central nervous system disease. Also brain specimens from MS patients and controls were obtained. Transcripts of various endogenous retroviruses in these samples were detected by RNA-PCR. RESULTS: Several endogenous retroviral sequences were transcribed in peripheral blood mononuclear cells and brain tissue from MS patients as well as controls. A composite transcript of an endogenous retrovirus and a zinc finger sequence was more frequently found in healthy donors than in MS patients. CONCLUSION: Some endogenous retroviruses are normally transcribed in white blood cells and brain tissue. The significance of those findings, which concerned the composite transcripts of the zinc finger sequence and its associated endogenous retrovirus is uncertain.

L11 ANSWER 20 OF 34 MEDLINE on STN

97317642. PubMed ID: 9174637. Cell cultures and associated retroviruses in multiple sclerosis. Collaborative Research Group on MS. **Perron H;** Firouzi R; Tuke P; Garson J A; Michel M; Beseme F; Bedin F; Mallet F; Marcel E; Seigneurin J M; Mandrand B. (BioMerieux S.A., UMR 103 CNRS-bioMerieux, Lyon, France.) Acta neurologica Scandinavica. Supplementum, (1997) 169 22-31. Journal code: 0370337. ISSN: 0065-1427. Pub. country: Denmark. Language: English.

AB Retroviral particles associated with reverse transcriptase (RT) activity in cell-cultures from MS patients have been reported by different groups. Cell-cultures have been used for the study and characterization of the corresponding retroviral genome which we have shown is related to ERV9 in the pol region. Previously unpublished details of a study with monocyte cultures are presented together with observations on leptomeningeal and choroid-plexus cultures. The generation of self-transformed cultures after inhibition of interferon, followed by the loss of retroviral expression and recurrent apoptosis, is analyzed. Retroviral particles with RT-activity are produced in monocyte cultures with an apparent correlation with MS disease activity. However, though leptomeningeal and choroid plexus cells from MS can be passaged for a limited period, their evolution in vitro is not compatible with stable retroviral expression. These culture limitations greatly hampered progress on the elucidation of the retroviral genome sequence.

L11 ANSWER 21 OF 34 MEDLINE on STN

97317641. PubMed ID: 9174636. Development of a pan-retrovirus detection system for multiple sclerosis studies. Tuke P W; **Perron H;** Bedin F; Beseme F; Garson J A. (Department of Virology, University College London Medical School, United Kingdom.) Acta neurologica Scandinavica. Supplementum, (1997) 169 16-21. Journal code: 0370337. ISSN: 0065-1427. Pub. country: Denmark. Language: English.

AB INTRODUCTION: Although recent claims implicating HTLV-1 in multiple sclerosis (MS) have been refuted, several reports suggest that another, hitherto uncharacterised, retrovirus may be involved. We have developed and applied a novel PCR-based strategy to explore this possibility. METHODS: Degenerate oligonucleotides were used in a semi-nested format to amplify, from reverse-transcribed RNA, a region of the pol gene which is well conserved amongst all known retroviruses. RESULTS: The 'pan-retrovirus' detection system was shown to be capable of detecting diverse retroviruses including human lentivirus, human oncovirus, simian

D-type virus and murine oncovirus. The 'pan-retrovirus' technique identified a novel retroviral sequence, designated MSRV-cpol, in the serum of an MS patient and also in purified virions from MS patient-derived tissue cultures. Sequence comparisons suggest that in the pol gene MSRV is related (approximately 75% homology) to the endogenous retroviral element ERV9. CONCLUSION: These findings lend further support to the concept of retroviral involvement in MS.

L11 ANSWER 22 OF 34 MEDLINE on STN

97191976. PubMed ID: 9044741. An electron microscopy study into the mechanism of gene transfer with lipopolyamines. Labat-Moleur F; Steffan A M; Brisson C; **Perron H**; Feugeas O; Furstenberger P; Oberling F; Brambilla E; Behr J P. (Laboratoire de Pathologie Cellulaire, CHU, Grenoble, France.) Gene therapy, (1996 Nov) 3 (11) 1010-7. Journal code: 9421525. ISSN: 0969-7128. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Cationic amphiphiles have been shown to mediate gene transfer to eukaryotic cells, although the nature and fate of the lipid-DNA complexes is still a matter of debate. Negative staining transmission electron microscopy (TEM) of the complexes in physiological medium, as well as thin-section TEM of transfected cells has been used to visualize the particles and the possible pathways leading to transgene expression. Lipopolyamines form a network of tubular micelles into which plasmid DNA is intertwined and condensed; the cationic particles contain hundreds of plasmid molecules and are heterogeneous with respect to size (0.1-0.5 microgram) and shape. Adherent cells (293M, 3T3, MRC5, primary leptomeningeal cells) take them up readily within minutes by spontaneous endocytosis. Among suspension cells, lymphocytes only incidentally show cytoplasmic inclusions and monocytes degrade the particles by phagocytosis. The marked decrease in transfection efficiency generally observed between adherent and nonadherent cells is thus due to reduce cell binding. This suggests that cationic particles bind to membrane components responsible for Ca2+-mediated cell anchoring to the extracellular matrix. Cation/anion-mediated endocytosis leads to endosomes that are entirely filled with the particles. Consequently, two escape mechanisms may operate: disruption of the lamellar envelope in close contact with tubular micelles, and endosome buffering by the lipopolyamine in response to proton entry, leading to osmotic swelling and endosome rupture. Even for moderately transfected MRC5 cells, 10(2)-10(3) particles are found either free or in cytoplasmic vacuoles 24 h after transfection, highlighting a very inefficient nuclear translocation process. Such high numbers are also the clue to the small concentration window between transfection and cytotoxicity that is often observed with nonviral vectors. Nuclear particle inclusions are sometimes seen, yet it is unclear whether plasmid uncoating (before expression) takes place by anion exchange in the cytoplasm or in the nucleus. The still lower efficiency of free plasmid translocation to the nucleus suggests an active role for the cationic lipid during this step. Although the last stages of the transfection mechanism remain unclear, the present work shows that the major barrier which hampers in vitro gene delivery with cationic vectors is nuclear translocation (and cell entry for nonadherent cells), providing precise targets for the design of improved nonviral vectors.

L11 ANSWER 23 OF 34 MEDLINE on STN

96306943. PubMed ID: 8762982. [Gliotoxic factor and multiple sclerosis]. Un facteur gliotoxique et la sclerose en plaques. Rieger F; Amouri R; Benjelloun N; Cifuentes-Diaz C; Lyon-Caen O; Hantaz-Ambroise D; Dobransky T; **Perron H**; Gemy C. (INSERM U. 153, equipe de neurobiologie et de neuropathologie fondamentales, Paris, France.) Comptes rendus de l'Academie des sciences. Serie III, Sciences de la vie, (1996 Apr) 319 (4)

343-50. Journal code: 8503078. ISSN: 0764-4469. Pub. country: France. Language: French.

AB Multiple sclerosis in a disease of the central nervous system characterized by perivascular and periventricular lesions of the myelin and immune cell infiltrates and increased permeability of the blood-brain barrier. We have found a cytotoxic factor of the cerebrospinal fluid (CSF) specific for multiple sclerosis patients which has 2 main characteristic effects in vitro on primary or immortalized astrocyte cultures: (1) disruption of the gliofilament network of the cells; and (2) apoptotic cell death induction. Moreover, in vivo, intraventricular injections of minute amounts of partially purified gliotoxic factor in adult rats have striking effects on both the morphology and general organization of astrocytes in the entire brain and the permeability characteristics of the blood brain barrier, which becomes leaky to immunoglobulins. These pathological effects are strongly similar to some of the neuropathological findings reported during the course of MS--They suggest an entirely new hypothesis to explain the active stage of the disease: the presence of a new factor of unknown extrinsic (viral) or intrinsic (cellular) origin, able to disorganize the glial cytoskeleton and glial cell differentiation. This factor is then able to provoke glial cell death. Such glial cell death may result in both demyelination and increased blood brain barrier permeability. Both in vitro and in vivo studies strongly support the idea that this gliotoxic factor plays a central role in the pathogenesis of MS, making its full identification a critical theme for MS research.

L11 ANSWER 24 OF 34 MEDLINE on STN

96059169. PubMed ID: 7595609. Sporadic ALS/MND: a global neurodegeneration with retroviral involvement?. Westarp M E; Ferrante P; **Perron H;** Bartmann P; Kornhuber H H. (Department of Neurology, University of Ulm, Germany.) Journal of the neurological sciences, (1995 May) 129 Suppl 145-7. Journal code: 0375403. ISSN: 0022-510X. Pub. country: Netherlands. Language: English.

AB Sporadic amyotrophic lateral sclerosis may be an aetiologically heterogenous disease. We confirmed elevated circulating IgG immune complexes, and altered IgG seroreactivities against human retroviral antigens (HIV-2 and HTLV immunoblots) in overlapping subgroups of patients. Together with preliminary findings of a positive polymerase chain reactivity for human T-lymphotropic virus (HTLV.tax/rex) in blood leukocytes of 5 out of 14 sALS patients, we interpret this as evidence for a retroviral involvement in this relentlessly progressive, often asymmetrically spreading neurodegeneration. The possibility of a secondary phenomenon seems unlikely, yet cannot be completely ruled out.

L11 ANSWER 25 OF 34 MEDLINE on STN

95025523. PubMed ID: 7939298. [Present status of retroviruses in human infectious disease]. Actualite des retrovirus en pathologie infectieuse humaine. Seigneurin J M; **Perron H.** (Laboratoire de virologie, Faculte de medecine de Grenoble, Domaine de la Merci, La Tronche.) La Revue du praticien, (1994 Apr 1) 44 (7) 888-93. Ref: 38. Journal code: 0404334. ISSN: 0035-2640. Pub. country: France. Language: French.

AB Retroviruses have been shown to be oncogenic in many animals for decades. In humans, retroviruses became worth of interest no sooner than in the early eighties. HIV is at the moment the last one of the well studied human retroviruses. Besides, HTLV-1, the prevalence of which is geographically restricted, is associated with adult T-cell leukemia/lymphoma, and with chronic myelopathies. This virus, as well as the closely related and rarer HTLV-2, is transmitted sexually, probably perinatally, and by infected blood and blood products. Among spumaviruses, an additional retrovirus subfamily, the human

spumaretrovirus (HSRV)--or human foamy virus--seems to have a low pathogenicity for human, although it is believed to be associated with Graves disease. Finally, endogenous retroviruses address new issues in humans, in particular with regard to relationship between virus and host genetic inheritance. These viruses could play a role in neurodegenerative or autoimmune diseases.

L11 ANSWER 26 OF 34 MEDLINE on STN
94078708. PubMed ID: 8256555. Do endogenous retroviruses have etiological implications in inflammatory and degenerative nervous system diseases?. Rasmussen H B; **Perron H**; Clausen J. (Institute of Life Sciences and Chemistry, Roskilde University, Denmark.) Acta neurologica Scandinavica, (1993 Sep) 88 (3) 190-8. Ref: 83. Journal code: 0370336. ISSN: 0001-6314. Pub. country: Denmark. Language: English.
AB Vertebrates carry large numbers of endogenous retroviruses (ERVs) and related sequences in their genomes. These retroviral elements are inherited as Mendelian traits. Generally, ERVs are defective without the ability of being expressed as viral particles. However, ERV sequences often have a potential for expression of at least some proteins. So far, the possible biological significance of ERVs is not clear. Nonetheless, there are observations suggesting a connection between ERVs and various diseases. This is the case with murine lupus and a spinal cord disease of certain mouse strains. In the present review, we discuss possible mechanisms by which ERVs could contribute to the development of human degenerative and inflammatory nervous system diseases, including direct effects on nervous system cells and immune cells. Interactions between ERVs and infectious viruses are also discussed. Finally, we review a possible retroviral etiology of multiple sclerosis.

L11 ANSWER 27 OF 34 MEDLINE on STN
93317047. PubMed ID: 8327019. Correlation analysis between bovine populations, other farm animals, house pets, and multiple sclerosis prevalence. Malosse D; **Perron H**. (Army Medical Research Center, La Tronche, France.) Neuroepidemiology, (1993) 12 (1) 15-27. Journal code: 8218700. ISSN: 0251-5350. Pub. country: Switzerland. Language: English.
AB In a previous study we analyzed the possible relationship between dairy product consumption and multiple sclerosis (MS) worldwide. We showed that a good correlation (Spearman rank $p = 0.836$), statistically strongly significant ($p < 0.0001$), existed between liquid cow milk consumption and MS prevalence. The interpretation of this strong correlation between MS and milk consumption is still unclear: fresh milk could be considered as a cofactor, but it could also reflect a much stronger association with MS of another unstudied factor, well correlated with milk consumption (yet, this is not the case for latitude). Obviously, the bovine population in each country and, particularly milk cows, has to be considered. In the present study, we analyze the correlations existing between the figures of national cow milk production and MS prevalence in 20 countries. We also analyze the correlations with the whole bovine, ovine, caprine, porcine, horse, poultry, cat and dog populations. Here again we find significant correlations between (i) cow milk production per inhabitant, (ii) national bovine density per inhabitant, and (iii) local bovine geographic density, and MS prevalence. However, these correlations are relatively weaker than that found with fresh liquid milk consumption in our previous study. No correlation is found with other farm animals or with pets in the same countries. The epidemiological significance of these results, suggesting a preponderant role of fresh cow milk, is discussed.

L11 ANSWER 28 OF 34 MEDLINE on STN
93180948. PubMed ID: 1291895. Correlation between milk and dairy product consumption and multiple sclerosis prevalence: a worldwide study. Malosse

D; **Perron H**; Sasco A; Seigneurin J M. (Laboratoire de Virologie, Faculte de Medecine, CHRU, Grenoble, France.) Neuroepidemiology, (1992) 11 (4-6) 304-12. Journal code: 8218700. ISSN: 0251-5350. Pub. country: Switzerland. Language: English.

AB Multiple sclerosis (MS) epidemiology suggests that different factors are involved in the clinical expression of the disease. Alimentary cofactors have already been considered, but mainly theoretically. We have studied the relationship between MS prevalence and dairy product consumption in 27 countries and 29 populations all over the world, with Spearman's correlation test. A good correlation between liquid cow milk and MS prevalence (rho = 0.836) was found; this correlation was highly significant ($p < 0.001$). A low but still significant correlation was obtained with cream or butter consumption (rho = 0.619 and rho = 0.504, respectively). No correlation was found for cheese. These results suggest that liquid cow milk could contain factor(s) - no longer present in the processed milk - influencing the clinical appearance of MS. The possible role of some dairy by-products is discussed in the light of a multifactorial etiology of MS.

L11 ANSWER 29 OF 34 MEDLINE on STN

93139785. PubMed ID: 7678635. Herpes simplex virus ICP0 and ICP4 immediate early proteins strongly enhance expression of a retrovirus harboured by a leptomeningeal cell line from a patient with multiple sclerosis. **Perron H**; Suh M; Lalande B; Gratacap B; Laurent A; Stoebner P; Seigneurin J M. (UMR 103 CNRS/Biomerieux, ENSL, Lyon, France.) Journal of general virology, (1993 Jan) 74 (Pt 1) 65-72. Journal code: 0077340. ISSN: 0022-1317. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A leptomeningeal cell line (LM7) harbouring an unknown retrovirus was recently isolated from the cerebrospinal fluid of a patient with multiple sclerosis. However, spontaneous expression of the LM7 retrovirus in this primary culture is quite low. We present results showing that in vitro infection of LM7 cells with herpes simplex virus type 1 (HSV-1), but not that of control cells, results in (i) potent stimulation of the specific reverse transcriptase (RT) activity detected in the culture supernatant and (ii) co-expression of both typical HSV-1 virions and abundant retrovirus-like particles. Transfection of LM7 cells with plasmids expressing HSV-1 immediate early (IE) ICP0 and ICP4 proteins produced a similar enhancement of RT activity in culture supernatants with retrovirus-like particles being identifiable by electron microscopy. These effects were not observed with a plasmid expressing ICP27 or with the parental plasmid in LM7 cells, nor with any of these four plasmids in control cells. These results show that HSV IE trans-activating proteins strongly enhance the expression of the latent retrovirus present in LM7 cells. The possible role in vivo of herpesviruses as 'triggering' cofactors in the retrovirus hypothesis for multiple sclerosis aetiology is also discussed.

L11 ANSWER 30 OF 34 MEDLINE on STN

93126664. PubMed ID: 1282730. In vitro transmission and antigenicity of a retrovirus isolated from a multiple sclerosis patient. **Perron H**; Gratacap B; Lalande B; Genoulaz O; Laurent A; Geny C; Mallaret M; Innocenti P; Schuller E; Stoebner P; +. (UMR 103 CNRS/BioMerieux, Ecole Normale Superieure de Lyon, France.) Research in virology, (1992 Sep-Oct) 143 (5) 337-50. Journal code: 8907469. ISSN: 0923-2516. Pub. country: France. Language: English.

AB We have recently isolated an apparently novel retrovirus (LM7) from a patient with multiple sclerosis (MS). We present here results showing that (1) LM7 retrovirus can be transmitted in vitro to a normal human leptomeningeal cell culture and that (2) specific antibody against this retroviral strain can be detected in MS cases. Our results suggest that,

if this virus is an endogenous retrovirus, it is different from human endogenous elements already described.

L11 ANSWER 31 OF 34 MEDLINE on STN
92170284. PubMed ID: 1724334. Antibody to reverse transcriptase of human retroviruses in multiple sclerosis. **Perron H**; Geny C; Genoulaz O; Pellat J; Perret J; Seigneurin J M. (Department of Virology, University Hospital, Grenoble, France.) Acta neurologica Scandinavica, (1991 Dec) 84 (6) 507-13. Journal code: 0370336. ISSN: 0001-6314. Pub. country: Denmark. Language: English.
AB HTLV-1, HIV-1 and HIV-2 western blot analysis of sera from patients with multiple sclerosis (MS), from patients with other neurological diseases and from blood donors, revealed a rather frequent cross-reactivity with retroviral proteins in the MS group, though no patient was positive with the corresponding specific ELISA serology. Statistical analysis revealed a significant difference between the MS group and the two control groups for HIV-1 and HIV-2 reverse transcriptase fragments and for HTLV-1 p24. The general significance of these observations is discussed in the light of a retroviral hypothesis for the aetiology of MS. It is suggested that, if a retrovirus is present in MS patients, it does not necessarily belong to the HTLV sub-family and could as well be a lentivirus, like Visna virus, the causative agent of a demyelinating disease in sheep which is one--natural--model for MS.

L11 ANSWER 32 OF 34 MEDLINE on STN
91194476. PubMed ID: 1707471. Isolation of retrovirus from patients with multiple sclerosis. **Perron H**; Lalande B; Gratacap B; Laurent A; Genoulaz O; Geny C; Mallaret M; Schuller E; Stoebner P; Seigneurin J M. Lancet, (1991 Apr 6) 337 (8745) 862-3. Journal code: 2985213R. ISSN: 0140-6736. Pub. country: ENGLAND: United Kingdom. Language: English.

L11 ANSWER 33 OF 34 MEDLINE on STN
90139926. PubMed ID: 2482522. Leptomeningeal cell line from multiple sclerosis with reverse transcriptase activity and viral particles. **Perron H**; Geny C; Laurent A; Mouriquand C; Pellat J; Perret J; Seigneurin J M. (Laboratoire de Virologie, Centre Hospitalier Universitaire, Grenoble, France.) Research in virology, (1989 Nov-Dec) 140 (6) 551-61. Journal code: 8907469. ISSN: 0923-2516. Pub. country: France. Language: English.
AB A leptomeningeal cell line (clonal but not immortal) was isolated from lumbar-punctured cerebrospinal fluid in a patient with definite multiple sclerosis (MS). This cell line, named LM7, was characterized by immunocytochemical and ultrastructural analyses and was found to produce specific viral reverse transcriptase activity, whereas electron microscopy revealed the presence of viral particles. This patient had no antibodies against human T-leukaemia virus type 1 (HTLV-I) or human immunodeficiency viruses types 1 and 2 (HIV-1, HIV-2). Moreover, monoclonal antibodies against HTLV-I and HIV-1 failed to recognize epitopes in induced LM7 cells. The possible relationship between MS and the virus present in LM7 cells is discussed.

L11 ANSWER 34 OF 34 MEDLINE on STN
88076253. PubMed ID: 3120656. [Meningococcal and rickettsial meningitis]. Meningite a meningocoques et rickettsioses. Jadin J B; Chabasse D; **Perron H**; Pouplard F; Granry J C. (Provinciaal Instituut voor Hygiene, Antwerpen.) Archives de l'Institut Pasteur de Tunis, (1987 Jul) 64 (3) 321-5. Journal code: 7502527. ISSN: 0020-2509. Pub. country: Tunisia. Language: French.

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                                                           ENTRY    SESSION
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 31 Mar 2005 (20050331/PD)
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>>>  the earliest to the latest publication.                           <<<

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> s (multiple sclerosis)
        962413 MULTIPLE
         22689 SCLEROSIS
L12      17472 (MULTIPLE SCLEROSIS)
                (MULTIPLE(W)SCLEROSIS)

=> s l12 adn (ERV or endogenous retrovir? or human endogenous retrovir? or HERV?)
MISSING OPERATOR L12 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l12 and (ERV/clm or MSRV?/clm or HERV/clm)
            10 ERV/CLM
             5 MSRV?/CLM
            11 HERV/CLM
L13         10 L12 AND (ERV/CLM OR MSRV?/CLM OR HERV/CLM)

=> d his

     (FILE 'HOME' ENTERED AT 12:06:09 ON 04 APR 2005)
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     FILE 'USPATFULL' ENTERED AT 12:06:16 ON 04 APR 2005
                E PARANHOS-BACCALA G/IN
L1           12 S E2
                E PERRON HERVE/IN
L2           22 S E3
L3           16 S L2 NOT L1
                E OTT CATHERINE/IN
                E MANDRAN BERNARD/IN
L4           47 S E5-E8
L5           30 S L4 NOT (L1 OR L2)

     FILE 'WPIDS' ENTERED AT 12:15:25 ON 04 APR 2005
                E PARANHOS BACCALA G/IN
L6           11 S E3
                E PERRON HERVE/IN
L7           24 S E2
L8           19 S L7 NOT L6

     FILE 'MEDLINE' ENTERED AT 12:18:10 ON 04 APR 2005
                E PARANHOS BACCALA G/AU
L9           30 S E2-E5
                E PERRON H/AU
L10          39 S E3 OR E7
L11          34 S L10 NOT L9

     FILE 'USPATFULL' ENTERED AT 12:19:56 ON 04 APR 2005
L12       17472 S (MULTIPLE SCLEROSIS)
L13          10 S L12 AND (ERV/CLM OR MSRV?/CLM OR HERV/CLM)

=> s l13 not (l1 or l2)
L14           3 L13 NOT (L1 OR L2)

=> d l14,cbib,ab,clm,1-3

L14  ANSWER 1 OF 3  USPATFULL on STN
2004:70905 Multiple sclerosis-related superantigen.
    Conrad, Bernard, Geneve, SWITZERLAND
    Mach, Bernard, Chambesy, SWITZERLAND
    US 2004054133 A1 20040318
    APPLICATION: US 2002-133036  A1  20020426 (10)
    DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     The invention relates to a protein or peptide having superantigen (SAg)
       activity, said protein or peptide comprising the ENV protein of the
       human endogenous retrovirus HERV-W, the surface protein (SU) and
       transmembrane (TM) sub-units thereof, and fragments of HERV-W ENV and
       its subunits, particularly C-terminal fragments, which possess
       superantigen activity.
CLM    What is claimed is:
       1. Protein or peptide having superantigen (SAg) activity, said protein
       or peptide comprising:  i) the amino acid sequence designated <<G>> or
       <<GT>>, as illustrated in FIG. 7 or FIG. 8;  ii) the surface protein
       portion (SU) of the polypeptide <<G>> or <<GT>> illustrated in FIG. 7 or
       8, or  iii) the surface protein (SU) and transmembrane portion (TM) of
       the polypeptide <<G>> illustrated in FIG. 7 or 8, or  iv) the
       transmembrane portion (TM) of the polypeptide <<G>> illustrated in FIG.
       7 or 8, or  v) a protein fragment consisting of at least 20 consecutive
       amino acids, and preferably at least 100 consecutive amino acids of
       protein (i), (ii), (iii) or (iv).
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2. Protein or peptide having superantigen (SAg) activity, said protein or peptide consisting of: i) the surface protein portion (SU) of the polypeptide <<G>> or <<GT>> illustrated in FIG. 7 or 8, or, ii) the surface protein (SU) and transmembrane portion (TM) of the polypeptide <<G>> or <<GT>> illustrated in FIG. 7 or 8, or iii) the transmembrane portion (TM) of the polypeptide <<G>> illustrated in FIG. 7 or 8, or iv) a protein having at least 95%, and preferably at least 98% homology with protein (i), (ii) or (iii), or v) a protein fragment consisting of at least 20 and preferably at least 100 consecutive amino acids of protein (i), (ii), (iii) or (iv).

3. Protein or peptide having superantigen (SAg) activity, said protein or peptide having the following formula: ##EQU3## wherein (a) is an amino acid residue, or a sequence of two or more amino acid residues, with the proviso that said sequence does not consist of any one of the signal sequences: MALPYHIFLFTVLLPSFTLT, MGLPYHIFLCSVLSPCFTLT, MALPYHIFLFTVVSPSFTLT (b) is a protein or peptide according to claim 1 or 2; (c) is an amino acid residue, or a sequence of two or more amino acid residues; <<x>>=0 or 1, <<z>>=0 or 1, provided that $(x+z)\geq 1$; <<y>>$\geq$1. and N and C indicate amino and carboxy terminals respectively.

4. Protein or peptide according to claim 3, wherein (b) is a protein or peptide according to claim 2.

5. Protein or peptide according to claim 4, wherein (b) is a fragment consisting of a stretch of at least 50 and preferably at least 100 consecutive amino acids comprised within amino acids 121 to 538 of the protein <<G>> illustrated in FIG. 7 or 8.

6. Protein or peptide according to claim 5, wherein (b) is: a fragment consisting of amino acids 121 to 538 of the protein <<G>> illustrated in FIG. 7 or 8, or a fragment consisting of amino acids 121 to 317 of the protein <<G>> illustrated in FIG. 7 or 8, or a fragment consisting of amino acids 121 to 350 of the protein <<G>> illustrated in FIG. 7 or 8, or a fragment consisting of amino acids 121 to 520 of the protein <<G>> illustrated in FIG. 7 or 8.

7. Protein having superantigen (SAg) activity, said protein being obtainable by i) introducing a nucleic acid encoding a protein according to any one of claims 1 to 6 into a mammalian cell under conditions appropriate to obtain expression of the said nucleic acid, ii) recovering the protein produced as a result of expression of the said nucleic acid.

8. Protein according to claim 7, wherein said mammalian cell is MHC Class II+.

9. Protein or peptide according to any one of claims 1 to 8 wherein the SAg activity is specific for Vβ6.7 and/or Vβ17 and/or Vβ21.3-TCR chains.

10. Protein or peptide according to claim 9 wherein the SAg activity is specific for Vβ6.7- and Vβ17-TCR chains.

11. Nucleic acid molecule coding for a protein according to any one of claims 1 to 10.

12. Nucleic acid molecule having the following formula:

5'$(A)_{x-}(B)_{y-}(C)_{z3}$' wherein (A) is a single nucleotide, or an oligonucleotide of at least two nucleotides, with the proviso that said oligonucleotide does not encode any one of the signal sequences: MALPYHIFLFTVLLPSFTLT, MGLPYHIFLCSVLSPCFTLT, MALPYHIFLFTVVSPSFTLT (B) is a nucleic acid according to claim 11 (C) is a nucleotide, or a nucleic acid sequence of at least two nucleotides; <<x>>=0 or 1, <<z>>=0 or 1, with the proviso that $(x+z)\geq 1$; <<y>>≥ 1.

13. Nucleic acid molecule according to any one of claims 11 or 12 comprising or consisting of the sequence illustrated in FIG. 9 or 10, or a fragment of said sequence having at least 50 nucleotides, or a sequence having at least 80%, and preferably at least 90% identity with the sequence illustrated in FIG. 9 or 10.

14. Nucleic acid molecule according to claim 13 comprising a chimeric gene wherein (A) and (C) include heterologous transcription regulatory regions operably linked to (B).

15. Nucleic acid molecule comprising a sequence complementary to a nucleic acid molecule according to any one of claims 11 to 14.

16. Nucleic acid molecule capable of hybridizing in stringent conditions with a nucleic acid molecules according to any one of claims 11 to 14.

17. Vector comprising a nucleic acid molecule according to any one of claims 11 to 16.

18. Antibodies capable of specifically recognising a protein or peptide according to any one of claims 1 to 10.

19. Antibodies according to claim 18 which have the capacity to block the SAg activity of said protein or peptide.

20. Cell-line transfected with and capable of expressing a nucleic acid molecule according to any one of claims 6 to 12.

21. Non-human cell transfected with and expressing a nucleic acid molecule according to any one of claims 11 to 17.

22. Cells according to claim 20 or 21 which are MHC Class II+ or MHC Class II-inducible.

23. Eukaryotic cell transfected with a nucleic acid according to claim 14.

24. Eukaryotic cell according to claim 23 which is MHC Class II+ MHC Class II-inducible, and which have the capacity to exhibit SAg activity.

25. Cell according to claim 24, wherein the SAg activity is specific for Vβ6.7 and/or Vβ17 and/or Vβ21.3-TCR chains

26. Process for the diagnosis of **Multiple Sclerosis** (MS), comprising specifically detecting, in a biological sample of human origin, one or more of the following: i) SAg activity specific for Vβ6.7 and/or Vβ17 and/or Vβ21.3-TCR chains ii) a protein according to any one of claims 1 to iii) DNA or mRNA encoding a protein according to any one of claims 1 to 10.

27. Process for the diagnosis of **Multiple Sclerosis** (MS), or for the

detection of a predisposition to MS, comprising: i) contacting a sample of genomic DNA from an individual, with nucleic acid primers suitable for the amplification, in a nucleic acid amplification reaction, of all or part of the genomic locus containing the **HERV**-w ENV gene, ii) performing amplification of the said genomic locus, iii) sequencing the thus amplified nucleic acid, the presence of nucleic acid encoding a protein according to any one of claims 1 to 10 and having superantigen activity, being indicative of the presence or susceptibility to, MS

28. Process for the diagnosis of **HERV**-W-associated disorders such as **Multiple Sclerosis** (MS) or for the detection of a predisposition to MS, comprising: i) contacting a sample of mRNA from an individual, with nucleic acid primers suitable for the amplification, in an RNA amplification reaction, of all or part of the RNA encoding a protein according to any one of claims 1 to 10, ii) performing amplification of the said RNA, iii) sequencing the thus amplified nucleic acid, the presence of nucleic acid encoding a protein according to any one of claims 1 to 10 and having superantigen activity, being indicative of the presence of, or susceptibility to, MS

29. Process for the diagnosis of MS, comprising a process according to claim 27 in association with a process according to claim 28.

30. Process for identifiying substances capable of binding to a retroviral superantigen associated with **Multiple Sclerosis**, comprising contacting a substance under test, optionally labelled with a detectable marker, with a protein according to any one of claims 1 to 10, and detecting binding.

31. Process for identifying, and optionally recovering, a substance capable of blocking SAg activity of a retroviral superantigen associated with **Multiple Sclerosis**, comprising i) introducing a substance under test into an assay system comprising MHC Class II+ cells functionally expressing a protein according to any one of claims 1 to 10, and cells bearing Vβ6.7-TCR chains, or cells bearing Vβ17-TCR chains, or cells bearing Vβ21.3-TCR chains, ii) determining the capacity of the substance under test to diminish or block Vβ stimulation by the retroviral superantigen, iii) optionally recovering the substance capable of blocking SAg activity of a retroviral superantigen.

32 Process for identifying, and optionally recovering, substances capable of blocking transcription or translation of **HERV**-W retroviral superantigen comprising: i) contacting a substance under test with cells expressing a protein according to any one of claims 1 to 10, and ii) detecting loss of SAg protein expression by means of a specific SAg protein marker, iii) optionally recovering the substance capable of blocking transcription or translation of the retroviral superantigen.

33. Kit for screening substances capable of blocking retroviral SAg activity associated with **Multiple Sclerosis**, or of blocking transcription or translation of the retroviral SAg protein, comprising: MHC Class II+ cells functionally expressing a retroviral SAg comprising a protein or peptide according to any one of claims 1 to 10: cells bearing Vβ6.7-TCR chains, or Vβ17-TCR chains, or Vβ21.3-TCR chains and means to detect specific Vβ stimulation by the retroviral SAg; optionally labelled antibodies specifically binding to the retroviral SAg.

34. Protein or peptide derived from a protein according to any one of claims 1 to 10, said protein or peptide being modified so as to be devoid of SAg activity and being capable of generating an immune response against **HERV**-W retroviral SAg.

35. Protein according to claim 34 which is a denatured, truncated or mutated form of a protein according to any one of claims 1 to 10, the mutation comprising deletion, insertion or replacement of at least one amino acid.

36 Protein according to claim 34 or 35 for use in therapy.

37. Vaccine comprising an immunogenically effective amount of a protein according to claim 34 or 35, in association with a pharmaceutically acceptable carrier and optionally adjuvant.

38. Nucleic acid molecule according to any one of claims 11 to 17 or a modified form of said molecule, for use as a prophylactic or therapeutic DNA vaccine against **Multiple Sclerosis**.

39. Substances identifiable by means of the process of any one of claims 31 to 33, for use in therapy and/or prevention of **Multiple Sclerosis**.

40. Use of substances capable of inhibiting or blocking the SAg activity of a protein according to any one of claims 1 to 10, for the preparation of a medicament for use in therapy and/or prevention of **Multiple Sclerosis**.

41. Transgenic non-human animal including in its genome a nucleic acid according to any one of claims 11 to 17.

42. Protein or peptide having superantigen (SAg) activity, comprising a protein having the formula (II): ##EQU4## wherein (a) is an amino acid sequence comprising or consisting of the signal sequence of the **HERV**-W ENV protein, or a part thereof, said part having at least five and preferably at least ten amino acids; (b) is an amino acid sequence comprising or consisting of the SU portion of the **HERV** W ENV protein or a part thereof, said part having at least fifty, preferably at least one hundred and most preferably at least one hundred and fifty amino acids; (c) is an amino acid sequence comprising or consisting of the TM portion of the **HERV** W ENV protein or a part thereof, said part having at least ten, preferably at least twenty and most preferably at least fifty amino acids; <<x>>=0 or 1, <<z>>=0 or 1; <<y>> is an integer ≥1; <<n>>=is an integer ≥1; and N and C indicate the amino and carboxy terminal respectively, with the proviso that the protein $[(a)_{x}-(b)_{y}-(c)_{z}]_{n}$ of Formula (II) does not consist of the full length SP-SU-TM **HERV**-W-ENV protein as illustrated for protein <<G>> in FIGS. 7 and 8.

42. Protein or peptide according to claim 41, wherein (a) comprises or consists of the signal sequence of the <<G>> or <<GT>> **HERV**-W ENV protein illustrated in FIGS. 7 or 8, or a part thereof, said part having at least five and preferably at least ten amino acids; (b) comprises or consists of the SU portion of the <<G>> or <<GT>> **HERV**-W ENV protein illustrated in FIGS. 7 or 8, or a part thereof, said part having at least fifty, preferably at least one hundred and most preferably at least one hundred and fifty amino acids, (c) comprises or consists of the TM portion of the <<G>> or <<GT>> **HERV**-W ENV protein illustrated in FIGS. 7 or 8, or a part thereof, said part having at least ten, preferably at least twenty and most preferably at least fifty amino

acids;

43. Nucleic acid encoding a protein or peptide according to claim 43.

L14 ANSWER 2 OF 3 USPATFULL on STN
2003:232063 Peptides derived from the superantigen (SAg) ENV protein of HERV-K18 and their use in obtaining SAG-inhibitory antibodies and in vaccination against SAG.
Dupuis, Marc, Geneva, SWITZERLAND
US 2003162263 A1 20030828
APPLICATION: US 2002-236091 A1 20020906 (10)
PRIORITY: US 2001-317703P 20010906 (60)
US 2001-317704P 20010906 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to peptides derived from the superantigen (SAg) ENV protein of the human endogenous retrovirus HERV-K18, and to the use of the peptides in obtaining antibodies which inhibit the superantigen activity of HERV-K18 ENV. The invention also relates to vaccine compositions for treating and preventing disorders associated with the ENV gene product of HERV-K18, for example autoimmune diseases such as insulin-dependent diabetes mellitus (IDDM). A preferred peptide consists of a portion of an N- or C-terminal segment of the HERV-K18.1 ENV protein, as illustrated in FIG. 1A, said N-terminal segment extending from amino acids 22 to 62 of HERV-K18.1 ENV, and said C-terminal segment extending from amino acids 110 to 153 of HERV-K18.1 ENV, wherein the peptide has a length of 6 to 40 amino acids and is capable of giving rise to antibodies which inhibit superantigen activity associated with HERV-K18 envelope proteins.

CLM What is claimed is:

1. A peptide comprising a portion of an N- or C-terminal segment of SEQ ID NO:1, said N-terminal segment extending from amino acids 22 to 62 of SEQ ID NO: 1; said C-terminal segment extending from amino acids 110 to 153 of SEQ ID NO: 1, and wherein said peptide has a length of 6 to 40 amino acids and is capable of giving rise to antibodies which inhibit superantigen activity associated with **HERV**-K18 envelope proteins.

2. The peptide of claim 1, having from 8 to 25 amino acids.

3. The peptide of claim 1, having from 10 to 20 amino acids.

4. The peptide of claim 1, wherein the N-terminal segment thereof extends from amino acids 22 to 50 of SEQ ID NO: 1.

5. The peptide of claim 1, wherein the N-terminal segment thereof extends from amino acids 22 to 42 of SEQ ID NO: 1.

6. The peptide of claim 1, wherein the C-terminal segment thereof extends from amino acids 110 to 145 of SEQ ID NO: 1.

7. The peptide of claim 1, wherein the C-terminal segment thereof extends from amino acids 112 to 140 of SEQ ID NO: 1.

8. The peptide of claim 1, wherein the C-terminal segment thereof extends from amino acids 112 to 135 of SEQ ID NO: 1.

9. The peptide of claim 1, comprising amino acids 22 to 32 of SEQ ID NO: 1.

10. The peptide of claim 1, comprising amino acids 116 to 131 of SEQ ID NO: 1.

11. The peptide of claim 1, comprising amino acids 116 to 130 of SEQ ID NO: 1.

12. The peptide of claim 1, comprising amino acids 113 to 127 of SEQ ID NO: 1.

13. The peptide of claim 1, which is capable of giving rise to antibodies which inhibit Vβ7 and/or Vβ13 SAg activity.

14. Antibodies specifically recognizing the peptide of claim 1, wherein said antibodies are capable of inhibiting SAg activity associated with **HERV**-K18 envelope proteins.

15. The antibodies of claim 14, which are capable of blocking Vβ7 and/or Vβ13 SAg activity.

16. The antibodies of claim 14, which are capable of blocking SAg activity from both alleles of the **HERV**-K 18 ENV gene in vivo.

17. The antibodies of claim 14, which are polyclonal.

18. The antibodies of claim 14, which are monoclonal.

19. The antibodies of claim 14, which are human or humanized.

20. A nucleic acid encoding the peptide of claim 1.

21. An immunogenic composition comprising the peptide of claim 1, or a mixture of peptides of claim 1.

22. A vaccine composition comprising the peptide of claim 1, or a mixture of peptides of claim 1, and a pharmaceutically acceptable carrier.

23. A vaccine composition comprising the nucleic acid of claim 20, and a pharmaceutically acceptable carrier.

24. A pharmaceutical composition comprising the antibodies of claim 14, or a mixture of said antibodies, and a pharmaceutically acceptable carrier.

25. A method for inhibiting superantigen activity associated with **HERV**-K18 envelope proteins in a subject, comprising administering the vaccine composition of claim 22 or the pharmaceutical composition of claim 24 to a subject.

26. A method for inhibiting superantigen activity associated with **HERV**-K18 envelope proteins in a subject, comprising administering the vaccine composition of claim 23 or the pharmaceutical composition of claim 24 to a subject.

27. A method for treating or preventing disorders associated with superantigen activity of **HERV**-K18 envelope proteins in a subject in need of such treatment, said method comprising the administration of the vaccine composition of claim 22, or the pharmaceutical composition of claim 24, to a subject.

28. A method for treating or preventing disorders associated with superantigen activity of **HERV**-K18 envelope proteins in a subject in need of such treatment, said method comprising the administration of the vaccine composition of claim 23, or a pharmaceutical composition of claim 24, to a subject.

29. The method of claim 27, wherein said disorder is an autoimmune disease.

30. The method of claim 29, wherein said disorder is insulin-dependent diabetes mellitus.

31. The method of claim 27, wherein said disorder is the result of a bacterial or viral infection.

32. A method for treating T-cell proliferation-related disorders in a subject, comprising the administration of the composition of claim 22 to a subject.

33. A method for treating T-cell proliferation-related disorders in a subject, comprising the administration of the composition of claim 23 to a subject.

34. A method for treating T-cell proliferation-related disorders in a subject, comprising the administration of the composition of claim 24 to a subject.

L14 ANSWER 3 OF 3 USPATFULL on STN
2003:152343 Retrovirus isolated from mantle histiocytes in mantle cell lymphoma

McGrath, Michael S., Burlingame, CA, UNITED STATES
Herndier, Brian, Burlingame, CA, UNITED STATES
US 2003104009 A1 20030605
APPLICATION: US 2002-222945 A1 20020815 (10)
PRIORITY: US 2001-312686P 20010815 (60)
DOCUMENT TYPE: Utility; APPLICATION.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention features an isolated, intact virus associated with human lymphoma, and originally isolated from a mantle cell lymphoma, referred to herein as a mantle histiocyte retrovirus (MHRV). The invention also features compositions and methods for detecting MHRV, as well as methods and compositions for propagating MHRV in vitro, screening for anti-MHRV agents, and generation of attenuated MHRV strains.

CLM What is claimed is:
1. An isolated mantle histiocyte retrovirus (MHRV) particle.

2. The isolated MHRV particle of claim 1, comprising an RNA genome encoding a GAG polypeptide comprising an amino acid sequence of amino acid residues 1-22 of SEQ ID NO: 8.

3. The isolated MHRV particle of claim 1, comprising an RNA genome characterized in that PCR amplification using a first primer comprising SEQ ID NO: 2 and a second primer comprising SEQ ID NO: 3 produces an amplification product of about 304 bp.

4. The isolated MHRV particle of claim 3, wherein the 304 bp amplification product comprises the sequence of SEQ ID NO: 1.

5. The isolated MHRV particle of claim 1, wherein the particle contains an RNA genome that, following infection and activity of viral reverse transcriptase, generates a cDNA that hybridizes under conditions of high stringency to a nucleic acid sequence of SEQ ID NO: 1.

6. The isolated MHRV particle of claim 1 comprising an RNA molecule comprising a sequence corresponding to SEQ ID NO: 1.

7. An isolated MHRV particle characterized by: being isolatable from a human lymphoma; having a particle diameter of from about 90 nm to 110 nm; having a membrane lipid bilayer; having an RNA genome visible by electron microscopy as a conical eccentric nucleoid; and having a GAG envelope polypeptide comprising amino acid residues 1-22 of the amino acid sequence of SEQ ID NO: 8.

8. An isolated MHRV particle characterized by: being isolatable from a human lymphoma; having a particle diameter of from about 90 nm to 110 nm; having a membrane lipid bilayer; and having an RNA genome visible by electron microscopy as a conical eccentric nucleoid; and wherein the RNA genome comprises a nucleic acid sequence corresponding to nucleotide residues 1-66 of SEQ ID NO: 7.

9. An isolated mammalian cell infected with the virus of claim 1.

10. The isolated mammalian cell of claim 9, wherein the cell is a macrophage.

11. An isolated mammalian cell infected with the virus of claim 8.

12. The isolated mammalian cell of claim 11, wherein the cell is a macrophage.

13. The isolated mammalian macrophage of claim 10 or 12, wherein the macrophage produces MHRV particles.

14. An isolated polynucleotide comprising a sequence encoding a polypeptide comprising an amino acid sequence of at least 4 contiguous amino acid residues of amino acid residues 1-22 of SEQ ID NO: 8.

15. The isolated polynucleotide of claim 14, wherein the polynucleotide comprises a sequence encoding a polypeptide comprising an amino acid sequence of at least 10 contiguous amino acid residues of amino acid residues 1-22 of SEQ ID NO: 8.

16. An isolated polynucleotide comprising a sequence of at least 12 contiguous residues of nucleic acid residues 1-66 of SEQ ID NO: 7.

17. The isolated polynucleotide of claim 16, wherein the polynucleotide comprises a sequence of at least 33 contiguous residues of nucleic acid residues 1-66 of SEQ ID NO: 7.

18. The isolated polynucleotide of claim 17, wherein the polynucleotide comprises a sequence of at least 50 contiguous residues of nucleic acid residues 1-66 of SEQ ID NO: 7.

19. The isolated polynucleotide of claims 14-18, wherein the polynucleotide is less than about 1 kb in length.

20. The isolated polynucleotide of claims 14-18, wherein the

polynucleotide is operably linked to a heterologous promoter element.

21. An isolated polynucleotide comprising a sequence that hybridizes under conditions of high stringency to at least a portion of the polynucleotide sequence of nucleotides 1-66 of SEQ ID NO: 7.

22. An isolated polynucleotide comprising a sequence having at least 65% identity to at least 12 contiguous nucleotides of nucleic acid residues 1-66 of SEQ ID NO: 7.

23. An isolated recombinant host cell containing the polynucleotide of any of claims 14 to 22.

24. An isolated vector containing the polynucleotide of any of claims 14 to 22.

25. An isolated MHRV GAG polypeptide.

26. An isolated polypeptide encoded by the polynucleotide of any of claims 14 to 22.

27. An isolated antibody that specifically binds the isolated MHRV GAG polypeptide of claim 25.

28. An isolated antibody that specifically binds the a polypeptide encoded by the polynucleotide of any of claims 14 to 22.

29. A method for detecting mantle histiocyte retrovirus (MHRV) in a sample, the method comprising: contacting a biological sample suspected of containing MHRV with an MHRV-specific probe, said contacting being for a time sufficient for binding of the MHRV-specific probe to the sample to form complexes between the probe and a probe target; and detecting the presence or absence of complexes of the MHRV-specific probe and the probe target in the sample; wherein detection of complexes in the sample indicates MHRV is present in the sample.

30. The method of claim 29, wherein the MHRV-specific probe and the probe target are nucleic acid, and wherein the MHRV-specific probe comprises at least 8 contiguous nucleotide residues of SEQ ID NO: 1.

31. The method of claim 29, wherein the MHRV-specific probe and the probe target are nucleic acid, and wherein the MHRV-specific probe comprises at least 8 contiguous nucleotide residues of residues 1-66 of SEQ ID NO: 7.

32. The method of claim 29, wherein the MHRV-specific probe is an MHRV-specific antibody and the probe target is an MHRV GAG polypeptide.

33. The method of claim 29, wherein the probe target is an anti-MHRV antibody and the MHRV-specific probe is a polypeptide comprising amino acid residues 1-22 of SEQ ID NO: 8.

34. The method of claim 29, wherein the biological sample is selected from the group consisting of blood, blood-derived products, plasma, and serum.

35. The method of claim 29, wherein the biological sample comprises a tissue containing a macrophage or a macrophage-derived tumor cell.

36. A method for detecting a mantle histiocyte retrovirus (MHRV) in a

sample, the method comprising: contacting a biological sample suspected of containing MHRV with a first MHRV-specific nucleic acid probe and with a second MHRV-specific nucleic acid probe, wherein the first probe and the second probe each comprise at least 15 contiguous nucleotides of a nucleic acid sequence of SEQ ID NO: 7 or complement thereof, said contacting being under conditions effective to produce an amplified DNA product; and detecting the presence or absence amplified DNA product; wherein detection of amplified DNA product corresponding to an amplified DNA product expected from a nucleic acid sequence comprising SEQ ID NO: 7 indicates the MHRV is present in the sample.

37. The method of claim 36, wherein the first probe comprises a sequence selected from the group consisting of **HERV**-9 and **HERV**-10

38. The method of claim 36, wherein the second probe comprises a sequence selected from the group consisting of **HERV**-8, **HERV**-11, and **HERV**-12.

39. The method of claim 36, wherein the first probe is **HERV**-8, the second probe is **HERV**-9, wherein detection of an amplified product of about 304 bp indicates MHRV is in the sample.

40. The method of claim 36, wherein the first probe is **HERV**-9 the second probe is **HERV**-12, wherein detection of an amplified product of about 1321 bp indicates MHRV is in the sample.

41. The method of claim 36, wherein the first probe is **HERV**-10 the second probe is **HERV**-11, wherein detection of an amplified product of about 1966 bp indicates MHRV is in the sample.

42. A kit for detection of mantle histiocyte retrovirus (MHRV), the kit comprising an MHRV-specific probe, wherein the probe is selected from the group consisting of: an MHRV-specific nucleic acid probe that specifically hybridizes to a sequence encoding an MHRV GAG polypeptide; an MHRV-specific GAG antibody; and an MHRV polypeptide that specifically binds an anti-MHRV GAG polypeptide.

43. A method of screening for anti-MHRV antiviral agents, the method comprising: contacting a candidate agent with a culture comprising a mammalian cell infected with MHRV, which cell produces viral particles; and detecting MHRV viral particles in supernatant of the culture; wherein a decrease in MHRV viral particles in the supernatant indicates that the candidate agent as activity as an anti-MHRV antiviral agent.

44. A method for detecting an MHRV-associated disease, the method comprising: contacting a biological sample with an MHRV-specific probe, wherein the biological sample was obtained from a subject suspected of having an MHRV-associated disease, said contacting being for a time sufficient for binding of the MHRV-specific probe to the sample to form complexes between the probe and a probe target; and detecting complexes of the MHRV-specific probe and the probe target in the sample; wherein detection of complexes in the sample indicates MHRV is present in the sample, which indicates the subject may have an MHRV-associated disease.

45. The method of claim 44, wherein the MHRV-associated disease is an MHRV-associated lymphoma.

46. The method of claim 44, wherein the MHRV-associated disease is selected from the group consisting of teratocarcinoma, **multiple sclerosis**, autoimmune rheumatic diseases, and schizophrenia.

47. A method for producing an MHRV GAG polypeptide of claim 25, the method comprising the steps of: a) culturing a recombinant host cell containing a recombinant MHRV GAG polypeptide-encoding polynucleotide sequence under conditions suitable for the expression of the polypeptide; and b) recovering the polypeptide from the host cell culture.

48. An immunogenic composition comprising an immunogenic polypeptide, wherein the immunogenic polypeptide comprises an amino acid sequence of amino acid residues 1-22 of a GAG polypeptide of mantle histiocyte retrovirus (MHRV).

49. An immunogenic composition comprising a nucleic acid molecule having a sequence encoding an immunogenic polypeptide, wherein the immunogenic polypeptides comprises an amino acid sequence of amino acid residues 1-22 of a GAG polypeptide of mantle histiocyte retrovirus (MHRV), and wherein the nucleic acid sequence is adapted for expression in a mammalian cell.

50. An isolated recombinant MHRV vector, the vector comprising: the MHRV polynucleotide of any of claims 14 to 22; at least one restriction site suitable for insertion of a heterologous nucleic acid; and a nucleic acid of interest comprising a sequence heterologous to the MHRV polynucleotide.

51. The isolated recombinant MHRV vector of claim 50, wherein the restriction site is non-naturally occurring in the MHRV genome.

52. An isolated recombinant MHRV particle comprising: a recombinant MHRV genome comprising the MHRV polynucleotide of any of claims 14 to 22 and further comprising at least one restriction site suitable for insertion of a heterologous nucleic acid.

53. The isolated recombinant MHRV particle of claim 52, wherein the recombinant MHRV genome further comprises a nucleic acid comprising a sequence heterologous to the MHRV polynucleotide, wherein the nucleic acid is operably inserted for expression in a host upon introduction of the MHRV vector into the host cell.

54. The isolated recombinant MHRV particle of claim 52, wherein the MHRV particle is replication-defective.

55. The isolated recombinant MHRV particle of claim 52, wherein the MHRV particle is replication competent.

=> d his

(FILE 'HOME' ENTERED AT 12:06:09 ON 04 APR 2005)

FILE 'USPATFULL' ENTERED AT 12:06:16 ON 04 APR 2005

```
                E PARANHOS-BACCALA G/IN
L1          12 S E2
                E PERRON HERVE/IN
L2          22 S E3
L3          16 S L2 NOT L1
                E OTT CATHERINE/IN
                E MANDRAN BERNARD/IN
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L4            47 S E5-E8
L5            30 S L4 NOT (L1 OR L2)

     FILE 'WPIDS' ENTERED AT 12:15:25 ON 04 APR 2005
                E PARANHOS BACCALA G/IN
L6            11 S E3
                E PERRON HERVE/IN
L7            24 S E2
L8            19 S L7 NOT L6

     FILE 'MEDLINE' ENTERED AT 12:18:10 ON 04 APR 2005
                E PARANHOS BACCALA G/AU
L9            30 S E2-E5
                E PERRON H/AU
L10           39 S E3 OR E7
L11           34 S L10 NOT L9

     FILE 'USPATFULL' ENTERED AT 12:19:56 ON 04 APR 2005
L12        17472 S (MULTIPLE SCLEROSIS)
L13           10 S L12 AND (ERV/CLM OR MSRV?/CLM OR HERV/CLM)
L14            3 S L13 NOT (L1 OR L2)

=> file medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    12.84     301.79

FILE 'MEDLINE' ENTERED AT 12:21:49 ON 04 APR 2005

 FILE LAST UPDATED: 2 APR 2005 (20050402/UP).  FILE COVERS 1950 TO DATE.

 On December 19, 2004, the 2005 MeSH terms were loaded.

 The MEDLINE reload for 2005 is now available.  For details enter HELP
 RLOAD at an arrow promt (=>).  See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

 OLDMEDLINE now back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2005 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s (multiple sclerosis)
        434607 MULTIPLE
         61877 SCLEROSIS
L15      30352 (MULTIPLE SCLEROSIS)
                (MULTIPLE(W)SCLEROSIS)

=> s l15 and (ERV or endogenous retrovir? or HERV? or human endogenous retrovir? or
          222 ERV
        128686 ENDOGENOUS
         34013 RETROVIR?
          1587 ENDOGENOUS RETROVIR?
                (ENDOGENOUS(W)RETROVIR?)
           891 HERV?
```

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       128686 ENDOGENOUS
        34013 RETROVIR?
          480 HUMAN ENDOGENOUS RETROVIR?
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L16        85 L15 AND (ERV OR ENDOGENOUS RETROVIR? OR HERV? OR HUMAN ENDOGENOU
              S RETROVIR? OR MSRV?)

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     11928120 PY<1999
L17        33 L16 AND PY<1999

=> d l17,cbib,ab,1-33

L17  ANSWER 1 OF 33     MEDLINE on STN
1999356477.  PubMed ID: 10427470.  Large number of polymorphic nucleotides
     and a termination codon in the env gene of the endogenous human retrovirus
     ERV3. Rasmussen H B; Clausen J. (Department of Life Science and Chemistry,
     Roskilde University, Denmark. ) Disease markers, (1998 Nov) 14 (3)
     127-33. Journal code: 8604127. ISSN: 0278-0240. Pub. country:
     Netherlands. Language: English.
AB   The terminal portion of the pol gene and the entire env gene of the
     human endogenous retrovirus ERV3 was screened for polymorphic
     nucleotides. For this purpose fragments amplified from the desired
     regions of ERV3 were subjected to single strand conformational analysis
     (SSCP analysis). Using this approach, we detected 13 polymorphic
     nucleotides, namely four in the pol gene and nine in the env gene. Three
     of the nucleotide substitutions were synonymous (not affecting the amino
     acid code). One of the non-synonymous nucleotide substitutions changed an
     arginine codon to a termination codon. The alleles at the different
     polymorphic sites could be arranged into five ERV3 haplotypes, two of
     which were new. To evaluate the possible significance of the termination
     codon, which precludes expression of a putative immunoregulatory factor,
     we examined samples of DNA from patients with multiple sclerosis, a
     demyelinating disease of presumed autoimmune etiology. We did not find an
     association between the ERV3 allele with the termination codon and this
     disease. Perhaps the presence of a stop codon combined with the high
     number of non-synonymous nucleotide substitutions in the reading frame of
     the env gene reflects absence of selective constraints during evolution.
     Obviously, our findings contradict the assumption that the reading frame
     of the ERV3 env gene has been conserved throughout evolution.

L17  ANSWER 2 OF 33     MEDLINE on STN
1999052087.  PubMed ID: 9835022.  Endogenous retroviruses and multiple
     sclerosis. II. HERV-7q. Alliel P M; Perin J P; Pierig R; Nussbaum J L;
     Menard A; Rieger F. (Inserm, Paris, France. ) Comptes rendus de l'Academie
     des sciences. Serie III, Sciences de la vie, (1998 Oct) 321 (10) 857-63.
     Journal code: 8503078. ISSN: 0764-4469. Pub. country: France. Language:
     English.
AB   The search for new endogenous retroviral sequences, on the basis of
     sequence homologies with the pol gene of the recently reported multiple
     sclerosis associated retrovirus (MSRV), allowed us to identify a full
     length endogenous retrovirus sequence located on the long arm of human
     chromosome 7. This retrovirus, HERV-7q, includes in its env region,
     within a single 1,620 bp open reading frame, a 664 bp domain almost
     identical to a 3' non-coding region of the rab7 gene. Transcripts
     encompassing both the env and the 3' LTR regions of HERV-7q have already
     been identified as expressed sequence tags, suggesting that this env-like
     gene might code for a 538 amino acid long deduced protein.
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L17 ANSWER 3 OF 33 MEDLINE on STN
1998441996. PubMed ID: 9769860. [**Endogenous retroviral** sequences analogous to that of the new retrovirus **MSRV** associated with **multiple sclerosis** (part 1)]. Sequences retrovirales endogenes analogues a celle du nouveau retrovirus **MSRV** associe a la sclerose en plaques (1re partie). Alliel P M; Perin J P; Belliveau J; Pierig R; Nussbaum J L; Rieger F. (Neurobiologie du developpement normal et pathologique, IFM, Paris, France.) Comptes rendus de l'Academie des sciences. Serie III, Sciences de la vie, **(1998 Jun)** 321 (6) 495-9. Journal code: 8503078. ISSN: 0764-4469. Pub. country: France. Language: French.

AB **Multiple sclerosis** (MS) is still of unknown origin and may involve autoimmune, genetic and viral components in a pathogenic sequence whose relative importance is yet to be determined. A peptide, isolated from the cerebrospinal fluid of MS patients, is similar to a fragment of the pol protein reverse transcriptase (RT) of the newly reported **MSRV** retrovirus. The 700 amino acid sequence of **MSRV**-RT is closely related to a novel human retroviral-like sequences. We also identified a gag-like sequence upstream of this human genomic RT-like sequence, which allowed us to identify altogether 4,000 nucleotides, possibly coding for an **endogenous retroviruses**. Homologous sequences found in other locations in the human genome seem to characterize a new family of retroviral endogenous sequences, which may be of relevance to **multiple sclerosis**.

L17 ANSWER 4 OF 33 MEDLINE on STN
1998434160. PubMed ID: 9763196. An **endogenous retrovirus** with nucleic acid sequences similar to those of the **multiple sclerosis** associated retrovirus at the human T-cell receptor alpha, delta gene locus. Alliel P M; Perin J P; Pierig R; Rieger F. (Neurobiologie du Developpement Normal et Pathologique, INSERM, IFM, Paris, France.) Cellular and molecular biology (Noisy-le-Grand, France), **(1998 Sep)** 44 (6) 927-31. Journal code: 9216789. ISSN: 0145-5680. Pub. country: France. Language: English.

AB Retroviruses are suspected to be involved in the pathogenesis of autoimmune diseases, such as **multiple sclerosis** (MS). Here, we describe a complete cartography of a novel **human endogenous retroviral** sequence with a pol domain which shares a high homology with the pol sequence of the **multiple sclerosis** associated retrovirus (**MSRV**). Since this new **endogenous retroviral** sequence is located in the close vicinity of the locus of the human gene coding for the T-cell receptor (TcR) alpha and delta chains on chromosome 14, it could be of potential interest for the understanding of MS pathogenesis.

L17 ANSWER 5 OF 33 MEDLINE on STN
1998430550. PubMed ID: 9759750. Expression of sequence variants of **endogenous retrovirus** RGH in particle form in **multiple sclerosis**. Christensen T; Dissing Sorensen P; Riemann H; Hansen H J; Moller-Larsen A. Lancet, **(1998 Sep 26)** 352 (9133) 1033. Journal code: 2985213R. ISSN: 0140-6736. Pub. country: ENGLAND: United Kingdom. Language: English.

L17 ANSWER 6 OF 33 MEDLINE on STN
1998426886. PubMed ID: 9754278. [**MSRV** retrovirus and gliotoxin protein: potential biological markers in **multiple sclerosis**?]. Retrovirus **MSRV** et proteine gliotoxique: marqueurs biologiques potentiels dans la sclerose en plaques?. Perron H. (Unite mixte CNRS-bioMerieux, Lyon.) Annales de biologie clinique, **(1998 Jul-Aug)** 56 (4) 427-38. Ref: 52. Journal code: 2984690R. ISSN: 0003-3898. Pub. country: France. Language: French.

AB The aetiopathogeny of **multiple sclerosis**, a neurological disease which prevalence and duration generate an important problem of public health in

industrialized countries where it is most frequent, is not clearly understood. The keys for the diagnosis and therapeutic strategies of MS are nonetheless dependent upon the identification of a well-defined aetiology and upon the understanding of the mechanisms and pathogenic connexions which lead to the demyelinating lesions of the central nervous system and to the dysfunctions of the immune system (autoimmunity) characteristic for the disease. The recent identification of a retroviral agent (**MSRV**) which produces extracellular particles detectable in the plasma, the CSF, and in some cell cultures from patients with MS, as well as of a cytotoxic factor targeting glial cells (gliotoxin) detected in parallel, could help elucidating the aetiopathogeny of MS. The usefulness of biological markers and targets derived from **MSRV** retrovirus and this gliotoxin, in the diagnostic and therapeutic perspectives for MS, is discussed in the light of the different aetiopathogenic hypotheses for the disease. From our results it is conceivable that a retroviral agent and pathogenic molecules such as this gliotoxin and an eventual **MSRV**-associated retroviral superantigen might initiate and perpetuate the cascade of events leading to MS. However, similar data on different simple retroviruses were recently published concerning autoimmune diseases such as diabetes type 1, Sjogren's syndrome and systemic lupus erythematosis, which could prefigurate a broader concept for the role of such retroviruses in the aetiopathogenesis of autoimmune diseases.

L17 ANSWER 7 OF 33 MEDLINE on STN

1998392693. PubMed ID: 9725072. Viruses and **multiple sclerosis**. Monteyne P; Bureau J F; Brahic M. (Institut Pasteur, Unite des Virus Lents, ERS 572 CNRS, Paris, France.) Current opinion in neurology, **(1998 Aug)** 11 (4) 287-91. Ref: 38. Journal code: 9319162. ISSN: 1350-7540. Pub. country: United States. Language: English.

AB Animal models illustrate how viruses and host genetic factors may interact to cause immune-mediated demyelination. Similar mechanisms may take place in at least some forms of **multiple sclerosis**, a disease that is histopathologically heterogeneous. No '**multiple sclerosis** virus' has been found yet, although recent data on human herpesvirus-6 antigens in **multiple sclerosis** brain warrant further investigation. **Multiple sclerosis** associated retrovirus, a recently described retroviral sequence isolated from **multiple sclerosis** material, is a member of the **endogenous retrovirus**-9 family. The association between the expression of this virus associated retrovirus and **multiple sclerosis** is only tentative.

L17 ANSWER 8 OF 33 MEDLINE on STN

1998255792. PubMed ID: 9596353. Detection of a gliotoxic activity in the cerebrospinal fluid from **multiple sclerosis** patients. Menard A; Pierig R; Pelletier J; Bensa P; Belliveau J; Mandrand B; Perron H; Rieger F. (INSERM Laboratoire de Neuromodulations Interactives et Neuropathologies - 17, Paris, France.) Neuroscience letters, **(1998 Mar 27)** 245 (1) 49-52. Journal code: 7600130. ISSN: 0304-3940. Pub. country: Ireland. Language: English.

AB We recently showed that peripheral blood cell supernatants from **multiple sclerosis** (MS) patients, containing reverse transcriptase activity and retroviral RNA from the newly human identified **multiple sclerosis** retrovirus (**MSRV**), also secrete a cytotoxin which induces death of primary mouse cortical glial cells. We have hypothesized that macrophages could release this cytotoxin in the cerebrospinal fluid. The cerebrospinal fluid cytotoxicity from 166 patients with various neurological diseases (including MS patients) was tested on glial cells in vitro. Our bioassay shows that a glial cytotoxic activity is significantly present in cerebrospinal fluid from patients with relapsing-remitting MS at relapse. Since this cytotoxic activity seems to

correlate with active cases of MS, it may represent a critical pathogenic factor in the neuropathology of MS.

L17 ANSWER 9 OF 33 MEDLINE on STN
1998214356. PubMed ID: 9553740. Haplotypes of the **endogenous retrovirus** HRES-1 in **multiple sclerosis** patients and healthy control subjects of Shanghai Chinese origin. Rasmussen H B; Kelly M A; Francis D A; Clausen J. (Department of Life Science and Chemistry, Roskilde University, Denmark.) Disease markers, **(1998 Feb)** 13 (4) 251-5. Ref: 21. Journal code: 8604127. ISSN: 0278-0240. Pub. country: Netherlands. Language: English.

L17 ANSWER 10 OF 33 MEDLINE on STN
1998201231. PubMed ID: 9540408. Retroelements in the human MHC class II region. Andersson G; Svensson A C; Setterblad N; Rask L. (Department of Cell Research, Uppsala Genetic Center, Swedish University of Agricultural Sciences, Sweden.. goran.andersson@cellfo.slu.se) . Trends in genetics : TIG, **(1998 Mar)** 14 (3) 109-14. Ref: 47. Journal code: 8507085. ISSN: 0168-9525. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Molecular genetic studies of the human major histocompatibility complex (MHC) have led to the identification of more than 200 genes. Besides the large number of genes in the MHC, densely clustered areas of retroelements have been identified. These include short and long interspersed elements (SINEs and LINEs), and **human endogenous retroviruses** (**HERVs**). The presence of retroelements in the MHC provides a clear example of how these elements affect the genome plasticity of the host. Comparative analyses of these retroelements have proven highly useful in evolutionary studies of the MHC. Recently, **HERV**-encoded superantigens have been implicated as candidate autoimmune genes in type I diabetes and **multiple sclerosis**. In addition, genetic analyses have revealed that autoimmune diseases show strong associations with MHC class II genes. The intriguing correlations between retroviral encoded antigens, MHC class II genes and the development of autoimmune disease merit intense future investigations of retroelements, in particular those **endogenous retroviruses** located in the MHC class II region proper.

L17 ANSWER 11 OF 33 MEDLINE on STN
1998163073. PubMed ID: 9504545. Virion-associated **MSRV**-RNA [correction of DNA] in **multiple sclerosis**. Poser C M. Lancet, **(1998 Mar 7)** 351 (9104) 755. Journal code: 2985213R. ISSN: 0140-6736. Pub. country: ENGLAND: United Kingdom. Language: English.

L17 ANSWER 12 OF 33 MEDLINE on STN
1998095013. PubMed ID: 9433428. Detection of virion-associated **MSRV**-RNA in serum of patients with **multiple sclerosis**. Garson J A; Tuke P W; Giraud P; Paranhos-Baccala G; Perron H. Lancet, **(1998 Jan 3)** 351 (9095) 33. Journal code: 2985213R. ISSN: 0140-6736. Pub. country: ENGLAND: United Kingdom. Language: English.

L17 ANSWER 13 OF 33 MEDLINE on STN
1998022594. PubMed ID: 9359636. A cytotoxic factor for glial cells: a new avenue of research for **multiple sclerosis**?. Menard A; Paranhos-Baccala G; Pelletier J; Mandrand B; Seigneurin J M; Perron H; Reiger F. (INSERM, Laboratoire de Neuromodulations Interactives et Neuropathologies, Paris, France.) Cellular and molecular biology (Noisy-le-Grand, France), **(1997 Sep)** 43 (6) 889-901. Journal code: 9216789. ISSN: 0145-5680. Pub. country: France. Language: English.
AB A novel retrovirus, provisionally called **Multiple Sclerosis** RetroVirus (**MSRV**), was recently described in **multiple sclerosis** (MS). We report here that monocyte/macrophage culture supernatants from MS patients

containing reverse transcriptase activity secrete a cytotoxin which induces death of primary mouse cortical glial cells. This cytotoxin, which was also found in MS cerebrospinal fluid, specifically causes death of mouse immortalized astrocytes and oligodendrocytes in vitro and seems to be associated to **MSRV**-specific RNA. This toxic factor, called gliotoxin, is present only in active cases of MS and is a stable glycosylated protein of 17 kDa, in CSF as well as in monocyte/macrophage culture supernatants. Since this gliotoxin is highly toxic for glial cells, it may represent an initial pathogenic factor, leading to the neuropathological features of MS, like blood brain barrier disruption and demyelination.

L17 ANSWER 14 OF 33 MEDLINE on STN

1998005317. PubMed ID: 9345457. Expression of **endogenous retroviruses** in blood mononuclear cells and brain tissue from **multiple sclerosis** patients. Rasmussen H B; Geny C; Deforges L; Perron H; Tourtelotte W; Heltberg A; Clausen J. (Institute of Life Sciences and Chemistry, Roskilde University, Denmark.) Multiple sclerosis (Houndmills, Basingstoke, England), **(1995 Jun)** 1 (2) 82-7. Journal code: 9509185. ISSN: 1352-4585. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The aim of the present study was to examine whether there is an abnormal expression of certain **endogenous retroviruses** in MS patients. For this purpose samples of peripheral blood mononuclear cells were obtained from 22 MS patients, a corresponding number of age and sex-matched healthy donors and five patients with other diseases affecting the central nervous system. In addition, brain specimens of macroscopic normal white and gray matter from four MS patients and a similar number of controls were included in the study. Using an enzymatic amplification technique, we found expression of the **endogenous retroviral** sequences, HRES-1, **HERV**-K10 and ERV3 in most samples of peripheral blood mononuclear cells from MS patients and controls without obvious differences between these two groups. In contrast, composite transcripts of ERV3 and a zinc finger sequence were more frequently detected in healthy donors than in MS patients. At present, the possible significance of this is uncertain. The retroviral element 4-1 was not transcribed or only transcribed at a very low level in peripheral blood cells of controls and MS patients. Transcripts of various **endogenous retroviruses** were also detected in the brain samples, but a different pattern was not apparent in the MS group as compared with controls. Aspects concerning a possible association between **endogenous retroviruses** and autoimmunity are considered.

L17 ANSWER 15 OF 33 MEDLINE on STN

1998005237. PubMed ID: 9345377. Possible association between **multiple sclerosis** and the human T cell leukemia virus (HTLV)-related endogenous element, HRES-1. Rasmussen H B; Heltberg A; Christensen K; Clausen J. (Institute of Life Sciences and Chemistry, Roskilde University, Denmark.) Multiple sclerosis (Houndmills, Basingstoke, England), **(1996 Oct)** 2 (3) 133-6. Journal code: 9509185. ISSN: 1352-4585. Pub. country: ENGLAND: United Kingdom. Language: English.

AB In the present study we searched for an association between the **human endogenous retroviral** element HRES-1 and **multiple sclerosis** (MS). Fragments of this **endogenous retrovirus** were amplified for subsequent examination by single strand conformational analysis. We did not find HRES-1 markers exclusively linked with MS and only the two already known polymorphisms, which define three alleles of HRES-1, were detected. However, we found a significant difference in the distribution of these alleles between a group of 87 MS patients and a control group of 158 healthy individuals (P = 0.014). There were no differences in the distribution of the HRES-1 allelic forms between MS patients with a

relapsing-remitting course and patients with chronic progressive MS. Our results provide evidence of an association between HRES-1 and MS. Possible explanations for this are discussed.

L17 ANSWER 16 OF 33 MEDLINE on STN

97447819. PubMed ID: 9303559. Gliotoxicity, reverse transcriptase activity and retroviral RNA in monocyte/macrophage culture supernatants from patients with **multiple sclerosis**. Menard A; Amouri R; Michel M; Marcel F; Brouillet A; Belliveau J; Geny C; Deforges L; Malcus-Vocanson C; Armstrong M; Lyon-Caen O; Mandrand B; Dobransky T; Rieger F; Perron H. (INSERM, Laboratoire de Neuromodulations Interactives et Neuropathologies, Paris, France.) FEBS letters, **(1997 Aug 25)** 413 (3) 477-85. Journal code: 0155157. ISSN: 0014-5793. Pub. country: Netherlands. Language: English.

AB In investigating a possible link between a novel retroviral agent (provisionally called **MSRV**), recently characterised in **multiple sclerosis** (MS), and the neuropathology of MS, it was found that there was a significant correlation between gliotoxicity and reverse transcriptase activity in monocyte/macrophage culture supernatants (MMCS) unique to MS patients. MMCS from healthy controls and patients with other neurological diseases did not display either gliotoxicity or reverse transcriptase activity. The observed gliotoxic effect was an initial, intermediate filament network disorganization and subsequent cell death which was specific to astrocytes and oligodendrocytes. The reverse transcriptase activity and **MSRV**-specific RNA were observed during the first 2 weeks of culture in MMCS from patients with active MS. The further elucidation of the molecular form(s) of this gliotoxic factor and its original source may be crucial in elucidating important etiopathogenic mechanisms in MS.

L17 ANSWER 17 OF 33 MEDLINE on STN

97352842. PubMed ID: 9207135. Molecular identification of a novel retrovirus repeatedly isolated from patients with **multiple sclerosis**. The Collaborative Research Group on **Multiple Sclerosis**. Perron H; Garson J A; Bedin F; Beseme F; Paranhos-Baccala G; Komurian-Pradel F; Mallet F; Tuke P W; Voisset C; Blond J L; Lalande B; Seigneurin J M; Mandrand B. (bioMerieux SA, Unite Mixte de Recherche 103, Centre National de la Recherche Scientifique-bioMerieux, 46, Allee d'Italie, 69364 Lyon Cedex 07, France.) Proceedings of the National Academy of Sciences of the United States of America, **(1997 Jul 8)** 94 (14) 7583-8. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The partial molecular characterization of **multiple sclerosis** (MS)-associated retrovirus (**MSRV**), a novel retrovirus previously called LM7, is reported. **MSRV** has been isolated repeatedly from leptomeningeal, choroid plexus and from Epstein-Barr virus-immortalized B cells of MS patients. A strategy based on reverse transcriptase PCR with RNA-purified extracellular virions yielded an initial pol fragment from which other regions of the retroviral genome were subsequently obtained by sequence extension. **MSRV**-specific PCR primers amplified a pol region from RNA present at the peak of reverse transcriptase activity, coinciding with extracellular viral particles in sucrose density gradients. The same sequence was detected in noncellular RNA from MS patient plasma and in cerebrospinal fluid from untreated MS patients. **MSRV** is related to, but distinct from, the **endogenous retroviral** sequence ERV9. Whether **MSRV** represents an exogenous retrovirus with closely related endogenous elements or a replication-competent, virion-producing, endogenous provirus is as yet unknown. Further molecular epidemiological studies are required to determine precisely the apparent association of virions containing **MSRV** RNA with MS.

L17 ANSWER 18 OF 33 MEDLINE on STN

97317644. PubMed ID: 9174639. Expression of **endogenous retroviruses** in blood mononuclear cells and brain tissue from **multiple sclerosis** patients. Rasmussen H B; Geny C; Deforges L; Perron H; Tourtelotte W; Heltberg A; Clausen J. (Institute of Life Sciences and Chemistry, Roskilde University, Denmark.) Acta neurologica Scandinavica. Supplementum, **(1997)** 169 38-44. Journal code: 0370337. ISSN: 0065-1427. Pub. country: Denmark. Language: English.

AB OBJECTIVES: To compare the expression of **endogenous retroviruses** in MS patients and controls. MATERIAL AND METHODS: Peripheral blood mononuclear cells were obtained from 22 MS patients, a corresponding number of matched healthy donors and five patients with other central nervous system disease. Also brain specimens from MS patients and controls were obtained. Transcripts of various **endogenous retroviruses** in these samples were detected by RNA-PCR. RESULTS: Several **endogenous retroviral** sequences were transcribed in peripheral blood mononuclear cells and brain tissue from MS patients as well as controls. A composite transcript of an **endogenous retrovirus** and a zinc finger sequence was more frequently found in healthy donors than in MS patients. CONCLUSION: Some **endogenous retroviruses** are normally transcribed in white blood cells and brain tissue. The significance of those findings, which concerned the composite transcripts of the zinc finger sequence and its associated **endogenous retrovirus** is uncertain.

L17 ANSWER 19 OF 33 MEDLINE on STN

97317643. PubMed ID: 9174638. Possible involvement of **endogenous retroviruses** in the development of autoimmune disorders, especially **multiple sclerosis**. Rasmussen H B; Clausen J. (Department of Life Sciences and Chemistry, Roskilde University, Denmark.) Acta neurologica Scandinavica. Supplementum, **(1997)** 169 32-7. Ref: 28. Journal code: 0370337. ISSN: 0065-1427. Pub. country: Denmark. Language: English.

AB **Endogenous retroviruses** are normal elements in vertebrate genomes. Many aspects concerning these genomic elements are still uncertain. In mice some **endogenous retroviral** sequences seem to be involved in the regulation of immune responses and there is even evidence that a retroviral element is responsible for the development of an autoimmune disease in a mouse strain. Whether **endogenous retroviruses** also contribute to the development of autoimmune diseases in humans is not known, but it is an interesting possibility. Below we briefly review **endogenous retroviruses** as potential etiological factors in autoimmunity and we discuss a possible association between MS and **endogenous retroviruses** on the basis of results from our laboratory.

L17 ANSWER 20 OF 33 MEDLINE on STN

97317641. PubMed ID: 9174636. Development of a pan-retrovirus detection system for **multiple sclerosis** studies. Tuke P W; Perron H; Bedin F; Beseme F; Garson J A. (Department of Virology, University College London Medical School, United Kingdom.) Acta neurologica Scandinavica. Supplementum, **(1997)** 169 16-21. Journal code: 0370337. ISSN: 0065-1427. Pub. country: Denmark. Language: English.

AB INTRODUCTION: Although recent claims implicating HTLV-1 in **multiple sclerosis** (MS) have been refuted, several reports suggest that another, hitherto uncharacterised, retrovirus may be involved. We have developed and applied a novel PCR-based strategy to explore this possibility. METHODS: Degenerate oligonucleotides were used in a semi-nested format to amplify, from reverse-transcribed RNA, a region of the pol gene which is well conserved amongst all known retroviruses. RESULTS: The 'pan-retrovirus' detection system was shown to be capable of detecting diverse retroviruses including human lentivirus, human oncovirus, simian D-type virus and murine oncovirus. The 'pan-retrovirus' technique

identified a novel retroviral sequence, designated **MSRV**-cpol, in the serum of an MS patient and also in purified virions from MS patient-derived tissue cultures. Sequence comparisons suggest that in the pol gene **MSRV** is related (approximately 75% homology) to the **endogenous retroviral** element ERV9. CONCLUSION: These findings lend further support to the concept of retroviral involvement in MS.

L17 ANSWER 21 OF 33 MEDLINE on STN

97025587. PubMed ID: 8871766. Three allelic forms of the **human endogenous retrovirus**, ERV3, and their frequencies in **multiple sclerosis** patients and healthy individuals. Rasmussen H B; Heltberg A; Lisby G; Clausen J. (Institute of Chemistry and Life Sciences, Roskilde University, Denmark.) Autoimmunity, **(1996)** 23 (2) 111-7. Journal code: 8900070. ISSN: 0891-6934. Pub. country: Switzerland. Language: English.

AB A possible association between the **endogenous retrovirus**, ERV3, and **multiple sclerosis** (MS) was examined. Samples of DNA from 74 MS patients and 159 healthy blood donors were subjected to enzymatic amplification followed by single strand conformational analysis to detect polymorphisms in the long terminal repeats of ERV3. Using this approach we detected six single base pair variations and a drop-out of a nucleotide. The linkage pattern of these base pair variations enabled us to define three allelic forms of ERV3. Polymorphisms exclusively present in the group of patients were not found and the distribution of the three allelic forms did not differ significantly between the group of controls and the MS group. Neither was there a significant difference in the distribution of the three alleles between MS patients with the progressive form and patients with relapsing/remitting MS. Our results are not in support of an association between ERV3 and MS.

L17 ANSWER 22 OF 33 MEDLINE on STN

96288154. PubMed ID: 8689767. Absence of human T-lymphotrophic virus type I in patients with systemic lupus erythematosus. Lipka K; Tebbe B; Finckh U; Rolfs A. (Neurochemical Research Laboratory, Free University of Berlin.) Clinical and experimental dermatology, **(1996 Jan)** 21 (1) 38-42. Journal code: 7606847. ISSN: 0307-6938. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The role of the human T-cell lymphotropic/leukaemia virus type I (HTLV-I) in the pathogenesis of autoimmune diseases of unknown cause, such as systemic lupus erythematosus (SLE), **multiple sclerosis** (MS) or Sjogren's syndrome (SS) has been discussed extensively. We have investigated whether SLE is in any way associated with exogenous HTLV-I. Using enzyme immunoassay (EIA), we found no seroreactivity against HTLV-I antigens in any of 24 SLE patients under investigation. Using a radioimmunoprecipitation assay (RIPA), there was also no expression of retroviral tax-protein demonstrable in 24 individuals with SLE. DNA preparations of peripheral blood cells, as well as isolated CD4- and CD8-positive cells, were examined for HTLV-I sequences (pol-, env-, gag-, LTR- and tax-region) using polymerase chain reaction (PCR). We were unable to demonstrate any specific HTLV-I PCR products in SLE specimens. Our data suggest that exogenous HTLV-I is not involved in the pathogenesis of SLE. Systemic lupus erythematosus (SLE) is a multisystem disease of unknown cause characterized by B-cell hyperactivity with hypergammaglobulinaemia and the formation of pathogenic autoantibodies. Patients may also show altered suppressor/helper T-cell ratios. Abnormalities in T-cell function include T-cell lymphopenia, expression of activation antigens and alteration of responses to mitogens and lymphokines. Human retroviruses are known to cause immune aberrations, such as diminished T-cell function and polyclonal B-cell stimulation, which are observed in patients with leukaemias, lymphomas and the acquired immunodeficiency syndrome (AIDS). Human T-cell lymphotropic/leukaemia

(HTLV-I) is aetiologically linked with adult virus type I T-cell leukaemia (ATL) and tropical spastic paraparesis. A common feature of the HTLV family is an LTR encoded protein (tax protein, p40tax) which triggers viral protein production in the early stages of a retroviral infection. Detection of p40tax may indicate transcriptional activity of a provirus. Several investigators have examined the possible involvement of HTLV-I in SLE and have produced conflicting results, especially so far as seroreactivity against HTLV-I antigens is concerned. The discovery of HTLV-I like particles in murine lupus might also indicate an important role of exogenous viruses in SLE. Olsen and colleagues describe a high seropositivity to anti-HTLV-I- and anti-HTLV-III antibodies and evidence of viral replication in patients with SLE. Lin et al. also demonstrated anti-HTLV-I antibodies in SLE patients. However, other authors failed to detect anti-HTLV-I antibodies, proviral structures or viral transcripts in SLE. We investigated whether or not there are any indications of the presence of the exogenous retrovirus, HTLV-I, in patients with SLE, at immunological and genetic levels. We found neither immunological nor molecular biological evidence for the existence of HTLV-I in SLE patients. There were some weak suggestions of the presence of possibly **endogenous retroviral** sequences.

L17 ANSWER 23 OF 33 MEDLINE on STN

96026385. PubMed ID: 7567836. [Superantigens and their implication in autoimmune diseases]. Super-antigenes et leur implication dans les maladies auto-immunes. Meyer O. (Clinique de Rhumatologie, Hopital Bichat, Paris.) Presse medicale (Paris, France : 1983), **(1995 Sep 2-9)** 24 (25) 1171-7. Ref: 28. Journal code: 8302490. ISSN: 0755-4982. Pub. country: France. Language: French.

AB Superantigens, unlike conventional antigens, are capable of stimulating cell growth and differentiation of a large proportion of T cells (10 -40%). There are two types of superantigens: **endogenous retroviral** superantigens (described only in mice) and bacterial superantigens. Bacterial superantigens are heat-resistant enterotoxins responsible for Staphylococcus food poisoning or toxic shock syndromes. T lymphocyte proliferation is associated with production of large quantities of cytokines, including interleukin-1, 2, 4, 6 and tumour necrosis factor which induce the symptoms observed in toxic syndromes. These superantigens form trimolecular complexes with the beta chains on the outer peptide pouch of class II HLA molecules and with certain families of V beta chains of the T-cell receptors on CD4 and CD8 lymphocytes. Unlike conventional antigens, superantigens do not have to be processed in small-sized peptides before presentation to T-cell receptors by the class II HLA molecules. The late consequences of T-cell activation by superantigens are either a deletion of the T-lymphocytes carrying V beta chains in families specific for a superantigen, or an anergy. The oligoclonal characteristic of T-lymphoid populations infiltrating the central nervous system, the synovial membrane or the salivary glands suggests that superantigens are implicated in the pathogenesis of certain autoimmune diseases such as **multiple sclerosis**, rheumatoid arthritis, and Sjogren's syndrome. Certain Staphylococcus superantigens could be the cause of Kawasaki's syndrome.

L17 ANSWER 24 OF 33 MEDLINE on STN

95260532. PubMed ID: 7537972. Isolation from human brain of six previously unreported cDNAs related to the reverse transcriptase of **human endogenous retroviruses**. Lefebvre S; Hubert B; Tekaia F; Brahic M; Bureau J F. (Unite des Virus Lents, UA 1157 Centre National de la Recherche Scientifique, Institut Pasteur, Paris, France.) AIDS research and human retroviruses, **(1995 Feb)** 11 (2) 231-7. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB cDNAs prepared from total RNA extracted from plaques of **multiple sclerosis** were amplified by the polymerase chain reaction. The 11-bp degenerate primers used were derived from conserved sequences of reverse transcriptase. Amplified cDNAs were fractionated according to size by electrophoresis in polyacrylamide gels under denaturing conditions. cDNAs of the proper size were cloned, grouped according to the sequence of their insert by differential hybridization, and sequenced. Six cDNAs were isolated and found to belong to new members of two groups of **human endogenous retroviruses**: the group related to ERV9 and that related to **HERVK10** and HUMMTV. These sequences were expressed in all human organs tested, including normal white matter of brain. The approach described in this article is a powerful tool with which to isolate new members of the reverse transcriptase gene family.

L17 ANSWER 25 OF 33 MEDLINE on STN

94078708. PubMed ID: 8256555. Do **endogenous retroviruses** have etiological implications in inflammatory and degenerative nervous system diseases?. Rasmussen H B; Perron H; Clausen J. (Institute of Life Sciences and Chemistry, Roskilde University, Denmark.) Acta neurologica Scandinavica, **(1993 Sep)** 88 (3) 190-8. Ref: 83. Journal code: 0370336. ISSN: 0001-6314. Pub. country: Denmark. Language: English.

AB Vertebrates carry large numbers of **endogenous retroviruses** (ERVs) and related sequences in their genomes. These retroviral elements are inherited as Mendelian traits. Generally, ERVs are defective without the ability of being expressed as viral particles. However, **ERV** sequences often have a potential for expression of at least some proteins. So far, the possible biological significance of ERVs is not clear. Nonetheless, there are observations suggesting a connection between ERVs and various diseases. This is the case with murine lupus and a spinal cord disease of certain mouse strains. In the present review, we discuss possible mechanisms by which ERVs could contribute to the development of human degenerative and inflammatory nervous system diseases, including direct effects on nervous system cells and immune cells. Interactions between ERVs and infectious viruses are also discussed. Finally, we review a possible retroviral etiology of **multiple sclerosis**.

L17 ANSWER 26 OF 33 MEDLINE on STN

93126664. PubMed ID: 1282730. In vitro transmission and antigenicity of a retrovirus isolated from a **multiple sclerosis** patient. Perron H; Gratacap B; Lalande B; Genoulaz O; Laurent A; Geny C; Mallaret M; Innocenti P; Schuller E; Stoebner P; +. (UMR 103 CNRS/BioMerieux, Ecole Normale Superieure de Lyon, France.) Research in virology, **(1992 Sep-Oct)** 143 (5) 337-50. Journal code: 8907469. ISSN: 0923-2516. Pub. country: France. Language: English.

AB We have recently isolated an apparently novel retrovirus (LM7) from a patient with **multiple sclerosis** (MS). We present here results showing that (1) LM7 retrovirus can be transmitted in vitro to a normal human leptomeningeal cell culture and that (2) specific antibody against this retroviral strain can be detected in MS cases. Our results suggest that, if this virus is an **endogenous retrovirus**, it is different from human endogenous elements already described.

L17 ANSWER 27 OF 33 MEDLINE on STN

93082293. PubMed ID: 1280512. The immune response to and expression of cross-reactive retroviral gag sequences in autoimmune disease. Brookes S M; Pandolfino Y A; Mitchell T J; Venables P J; Shattles W G; Clark D A; Entwistle A; Maini R N. (Division of Clinical Immunology, Kennedy Institute of Rheumatology, London.) British journal of rheumatology, **(1992 Nov)** 31 (11) 735-42. Journal code: 8302415. ISSN: 0263-7103. Pub. country: ENGLAND: United Kingdom. Language: English.

AB To examine the immune response to retroviral gag sequences in autoimmune disease, we measured antibody levels to synthetic peptides representing the major epitopes on HTLV-1 p19 gag and a homologous sequence on the **endogenous retrovirus**, HRES-1, in sera from 121 patients with autoimmune disease and 52 healthy controls. In the absence of HTLV-1 antibodies, using a conventional diagnostic assay, significantly elevated levels of antibodies to the HTLV-1 peptide were found in 23% of **multiple sclerosis** and 20% of anti-Sm antibody positive systemic lupus erythematosus patients. Elevated antibody levels to HRES-1 were found in 32% of Sjogren's syndrome and 19% of **multiple sclerosis** patients. Evidence of reactivity with both HTLV-1 and HRES-1 was found in human sera and cross-reactivity demonstrated with affinity purified rabbit anti-peptide antibodies. Expression of HRES-1, detected by antibodies and Northern blots, was found in lymphoblastoid cells, salivary gland biopsy sections and salivary gland epithelial cells in culture. This study confirms previous reports of low levels of anti-retroviral gag antibodies in autoimmune disease. The cross-reactions support the concept that reports of elevated HTLV-1 antibodies may be due to an endogenous agent such as HRES-1. The expression of HRES-1 salivary gland may explain its antigenicity in a small proportion of Sjogren's syndrome patients as well as suggesting mechanisms whereby it may contribute to the chronic inflammation of autoimmune disease.

L17 ANSWER 28 OF 33 MEDLINE on STN

92371528. PubMed ID: 1505588. Polymerase chain reaction analysis for specific HTLV-1 sequences from cerebrospinal fluid and peripheral blood cells in Sardinian **multiple sclerosis** patients. Marrosu M G; Mazzoleni A P; Galantuomo S; Melis A; Muntoni F; Lai E. (Istituto di Neuropsichiatria Infantile, Universita di Cagliari, Italia.) European neurology, **(1992)** 32 (4) 195-8. Journal code: 0150760. ISSN: 0014-3022. Pub. country: Switzerland. Language: English.

AB Using polymerase chain reaction and specific primers, we found no gag and env sequences of HTLV-1 in DNA samples from peripheral blood mononuclear cells of 26 **multiple sclerosis** (MS) patients with relapsing-remitting, relapsing-progressive and progressive course from onset of the disease, and from 8 patients affected with other neurological diseases (OND). A Positive signal for the gag region was found in DNA samples from cerebrospinal fluid mononuclear cells (CSFMC) of 6/17 (27.3%) MS patients (either with relapsing-remitting, or relapsing-progressive and progressive course from onset of the disease), and in 2/11 (18.2%) CSFMC OND samples. Positive hybridization for the env sequence was evident in 2/11 (18.2%) CSFMC from OND and none of MS samples. The finding of positive hybridization for gag and env sequences in a few samples of CSFMC may be related to the presence in the CSF of a great number of activated cells, which could express cross-reacting sequences of **endogenous retrovirus**.

L17 ANSWER 29 OF 33 MEDLINE on STN

92336466. PubMed ID: 1321526. [Disseminated sclerosis and retrovirus]. Dissemineret sklerose og retrovirus. Moller-Larsen A; Sommerlund M; Haahr S. (Institute for Medicinsk Mikrobiologi, Aarhus Universitet.) Ugeskrift for laeger, **(1992 Jun 8)** 154 (24) 1691-4. Ref: 22. Journal code: 0141730. ISSN: 0041-5782. Pub. country: Denmark. Language: Danish.

AB **Multiple sclerosis** is a disease characterized by neurologic dysfunction due to focal CNS lesions with demyelination. The cause of the disease is unknown; but it may be due to a virus and/or autoimmune reactions. The latter cause is suspected on account of family- and ethnical studies, the first on account of locally produced antibodies in the cerebrospinal fluid, and also epidemiologic investigations. The newly discovered human retroviruses, especially HTLV-I which is the cause of tropical spastic paraparesis, has been suspected as a possible cause; but

this has been disproved by multiple antibody- and PCR-studies. An uncharacterized exogenous or an **endogenous retrovirus** is still considered to be a possible cause or possibly partial cause of the disease which could be multifactorial.

L17 ANSWER 30 OF 33 MEDLINE on STN
92179297. PubMed ID: 1347429. Human T-cell lymphotropic virus (HTLV)-related endogenous sequence, HRES-1, encodes a 28-kDa protein: a possible autoantigen for HTLV-I gag-reactive autoantibodies. Banki K; Maceda J; Hurley E; Ablonczy E; Mattson D H; Szegedy L; Hung C; Perl A. (Department of Molecular Medicine and Immunology, Roswell Park Memorial Institute, Buffalo, NY 14263.) Proceedings of the National Academy of Sciences of the United States of America, **(1992 Mar 1)** 89 (5) 1939-43. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The presence of a human T-cell lymphotropic virus (HTLV)-related endogenous sequence, HRES-1, in the human genome has been documented. The HRES-1 genomic locus is transcriptionally active and contains open reading frames. Antibodies 232 and 233, specific for synthetic peptides pep14-24 and pep117-127, corresponding to two nonoverlapping HTLV-related regions in the longer open reading frame of HRES-1, recognize an identical 28-kDa protein in H9 human T cells. Thus, HRES-1 is a **human endogenous retroviral** sequence capable of protein expression. HRES-1/p28 is localized to the cytoplasm and nuclear bodies. While HTLV-I-specific antibodies react with HRES-1 peptides, antibody 233 cross-reacts with HTLV-I gag p24 protein. Three consecutive highly charged amino acid residues, Arg-Arg-Glu, present in both HRES-1 pep117-127 and HTLV-I gag p24 are likely to be the core of cross-reactive epitopes. The prevalence of antibodies to HRES-1 peptides pep14-24 and pep117-127 was determined in 65 normal blood donors and 146 patients with immunological disorders. Sera of patients with **multiple sclerosis** (19 out of 65, 29%), progressive systemic sclerosis (4 out of 17, 23%), systemic lupus erythematosus (4 out of 19, 21%), and Sjogren syndrome (2 out of 19, 10%) contained significantly higher HRES-1 peptide binding activity than sera of normal donors. Sera of patients with AIDS showed no specific binding to HRES-1 peptides. Nine of 30 HRES-1-seropositive patients showed immunoreactivity to HTLV-I gag p24. The data indicate that HRES-1/p28 may serve as an autoantigen eliciting autoantibodies cross-reactive with HTLV-I gag antigens.

L17 ANSWER 31 OF 33 MEDLINE on STN
91254022. PubMed ID: 2042954. **Multiple sclerosis**, human T-lymphotropic virus type I, and **human endogenous retrovirus** sequences. Cabirac G F; Ries D; Murray R S. Annals of neurology, **(1991 Mar)** 29 (3) 343-4. Journal code: 7707449. ISSN: 0364-5134. Pub. country: United States. Language: English.

L17 ANSWER 32 OF 33 MEDLINE on STN
86175005. PubMed ID: 3007991. **Endogenous retrovirus** in **multiple sclerosis**?. Kurth R. Nature, **(1986 Mar 20-26)** 320 (6059) 219-20. Journal code: 0410462. ISSN: 0028-0836. Pub. country: ENGLAND: United Kingdom. Language: English.

L17 ANSWER 33 OF 33 MEDLINE on STN
64152825. PubMed ID: 14194793. [FRONTAL LEUKOENCEPHALOPATHY IN SHEEP CAUSED BY CHRONIC APPLICATION OF AN ANALYTICAL REAGENT (P-NITROBENZENE-AZO-ALPHA-NAPHTHOL) REACTING WITH MAGNESIUM]. FRONTALE LEUKOENZEPHALOPATHIE DER SCHAFE, **HERVORGERUFEN** DURCH CHRONISCHE APPLIKATION EINES MIT MAGNESIUM REAGIERENDEN ANALYTISCHEN REAGENZ (P-NITROBENZOL-AZO-ALPHA-NAPHTHOL). HERMANOVA M; VAVRINEK J; NOVAKOVA S.

Zentralblatt fur allgemeine Pathologie und pathologische Anatomie, **(1964 Apr 20)** 105 470-8. Journal code: 9105593. ISSN: 0044-4030. Pub. country: GERMANY: Germany, Federal Republic of. Language: German.

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